Mental disorders
Children and adolescents screening and prevention

This document presents the summary and recommendations of the group of experts compiled by Inserm as part of a collective expertise procedure in order to respond to questions raised by the Caisse nationale d'assurance maladie des travailleurs indépendants (Canam, French National Sickness and Maternity Insurance for Self-Employed Persons in Non-Agricultural Professions) on the detection and prevention of mental disorders in children and adolescents.

The Centre d'expertise collective de l'Inserm (Inserm Collective Expertise Centre) has co-ordinated this collective expertise strategy with the Département animation et partenariat scientifique (Daps, Leadership and Scientific Partnership Department) for the preparation of this dossier in conjunction with the Service de documentation du Département de l'information scientifique et de la communication (Disc, Documentation Service of the Scientific Information and Communication Department) for the bibliographical research.

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Foreword

Mental health is an essential component of human health. A by no means insignificant proportion of children and adolescents (approximately 12 % in France) suffer from mental disorders, that is disorders in certain of their mental activities, which interfere with their development, slow down their education and compromise their future by repercussions on their day to day quality of life.

According to the World Health Organisation mental disorders are to increase by 50 % in 2020, to become, on the international level, one of the five main causes of morbidity in children. This increase is regarded as the crisis of the XXIst century.

Requests for paedophsychiatric treatment are frequently made late, although early management seems essential for prognosis. It would appear to be necessary, therefore, to learn to recognise these disorders in children as early as possible, in the various places that are there to receive them.

Canam wished to question Inserm, through the procedure of the expert panel report, in order to extract those elements allowing improved detection and prevention of mental disorders in children and adolescents, on the basis of data that has been validated at the international level. Taking the scope of the subject into account Inserm has, with the agreement of the client institution, directed the expert panel report towards those disorders that appear to be the best defined in the references: autism, hyperactivity obsessive-compulsive disorders, anxiety disorders, affective disorders, eating disorders, schizophrenia. Behavioural disorders, which represent a significant part of mental disorders, have not been taken into consideration because they are tackled in other documents produced by the expert panel. Thus, this expert panel report does not presume to tackle the whole of clinical practice in child and adolescent psychiatry.

In order to respond to the defined aims, Inserm has set up an expert group bringing together a broad range of medical and scientific fields to take on the various cross-disciplinary aspects of the subject at issue (descriptive and analytical epidemiology, neurobiology, imaging, cognition, clinical psychiatry, psychology) as well as to undertake a critical analysis of the studies performed on an international level in the field of the detection and prevention of the various mental disorders treated in this expert panel report.

The group structured its analysis around the following questions:

- What are the data on prevalence of the various mental disorders in children and adolescents, in France in particular?
- What are the various risk factors? What impact do perinatal complications have on the development of mental disorders? What role does familial and social environment play in the normal and pathologic development of children?
- What are the current data in genetic epidemiology on hereditary risk factors? What are the results of molecular genetic studies on the genes likely to be implicated?
- What are the neurobiological data on the development of the nervous system and the gene-environment interactions in this development?
- What are the recent data in cognitive neuroscience and the contribution of imaging techniques?
- What are the warning signs for the pathologies treated in this expert panel report: autism, hyperactivity, obsessive-compulsive disorders, anxiety disorders, affective

disorders, eating disorders, schizophrenia?

- Which tools are available for researching disorders in the general population? Which means of prevention have currently been evaluated?

Database research (Medline, Pascal, PsycINFO, Excerpta Medica) has led to the selection of almost 3,000 articles.

In the course of thirteen working sessions organised between the months of May 2000 and September 2001, the experts presented a critical analysis and a summary of studies published on the international level on mental disorders in children and adolescents. The last sessions focused on drafting the main conclusions and recommendations. Lastly, papers tackle different aspects of the follow-up of mental health in children and adolescents, in France and abroad.

Summary

As an introduction to the summary, the expert group wishes to draw attention to the fact that psychiatry is distinguished from other medical specialisms by certain features. In clinical practice, the evaluation of psychiatric disorders is more subjective in character than that of other disorders, which can be validated by laboratory assay or measurement of a functional marker (blood pressure for example).

Definitions of mental disorders and the criteria that define them are based, in essence, on the consensus of a community of specialists. The classifications that have been drawn up, such as the diagnostic tools DSM-IV and ICD-10, have been amended several times as new knowledge has been acquired. Mental disorders, even as defined today on the basis of internationally recognised criteria, differ greatly in their aetiopathogenesis. This is why the term "illness", which generally implies an aetiological mechanism, will not be used. Furthermore, the categorical approach to these classifications does not always take into account the continuum of intermediate cases, with incomplete or atypical symptomatology.

An analysis of data from the international literature brings to light multiple factors that are likely to play a role in the occurrence of mental disorders. Caution is required, however, in establishing causal connections, as many of these factors may be causes as well as consequences of the disorder in question, or may be only indirectly related to it.

Finally, the question of interactions between the environment, including the child's relational and emotional environment and factors of genetic predisposition lies at the heart of the debate. This expert panel report aims to put these data into the context of recent scientific advances, which open up promising perspectives for the understanding of mental disorders in children and adolescents.

Epidemiology in the area of mental disorders requires validated tools

Epidemiology allows us to study the frequency of diseases in various population groups (descriptive epidemiology), to investigate risk factors (analytical epidemiology) and to evaluate preventative or therapeutic interventions (interventional or evaluative epidemiology).

The aims of descriptive epidemiology are as follows: to measure the prevalence (current cases) and incidence (new cases) of disorders in a given population, and to follow their course; to describe the clinical features of these disorders as well as their distribution (by age, gender) and to use these data to identify priority groups for prevention or management. It is important to distinguish between studies performed on specific populations and those performed on representative samples of the general population. Population studies are easier to perform in small communities, such as the Isle of Wight, where a study was performed on all children aged from 10 to 12 years. Some longitudinal studies examining the development of cohorts of children followed from birth to adulthood have provided data on the incidence of mental disorders at different ages and, thanks to a prospective measurement of risk factors, on the biological, psychological and social mechanisms leading to psychopathologic development and its manifestations. The quality of data depends on the precision of the definitions employed, the sources of information, the nature of the populations studied, survey methods and diagnostic tools. The methodology of psychiatric surveys has become

more sophisticated nowadays as regards sampling techniques and data analysis. Many instruments and evaluation methods have been developed for psychiatric epidemiology in children and adolescents, which may also be employed for clinical research.

Every classification in the area of mental health has its limitations since, despite the need for one, no gold standard exists. The categorical classification of the *Diagnostic and statistical manual of mental diseases* (DSM) established for adults by the American Association of Psychiatry categorises individuals as normal or pathologic. The dimensional classification (for example the CBCL, *Child behavior checklist*) places children on an emotional or behavioural continuum, which ranges from the most normal to the most pathologic. Although established on different theoretical bases, the two types of classification share a similar symptomatology and an approach based on the number of symptoms or criteria, which leads to definitions of scores and thresholds. The DSM classification, used in the majority of international studies published in English, is in fact the reference classification for mental illness. This has the advantage, on the epidemiological level, of making it possible to compare the results of a large number of studies. The international classification of diseases (ICD-10) from the World Health Organisation, which is also not specific to children, establishes correspondences with the DSM classification. These instruments of psychopathologic evaluation have been successfully tested in several cultural contexts. The transcultural nature of a classification, however, is not universally recognised. The classification of mental disorders in children and adolescents used in France (CFTMEA, Classification des troubles mentaux de l'enfant et de l'adolescent), which is inspired by psychoanalytical theories, is used mainly in clinical practice and little in research, even if a certain degree of equivalence permits comparisons with ICD-10.

In France, one child out of eight has a mental disorder

The epidemiological studies performed in the last thirty-five years, mainly in developed countries, are essentially cross-sectional studies permitting an estimate of global morbidity connected with mental disorders. These surveys are often based on a two-phase protocol. In the first phase, all children selected are screened for disorders through the medium of questionnaires filled out by their teachers, parents and, from the age of 11 years onwards, the adolescents themselves. In a second phase, children with high or low scores take part in a phase of more extensive interviews intended to establish whether a mental disorder is present or not, and to measure the sensitivity and specificity of the screening instruments. In the second phase trained personnel (whether clinicians or not) are needed to perform the survey and diagnostic instruments of proven reliability and validation are required. Participation rates in these surveys are generally very high. Prevalence rates are reported for 3 to 12-month periods before the survey, or sometimes over the whole of a subject's life.

The prevalence of common mental disorders (including behavioural disorders) varies from 5 % to 25 %. The mean rate obtained on the basis of results from 49 surveys has been estimated at 12.5 %. A French survey in school-age children has yielded a very similar estimate (12.4 %). These rates concern two large groups of disorders, emotional (anxiety disorders, affective disorders) and behavioural (ADHD, oppositional defiant disorders), whose frequency is almost comparable and is close to 5 % to 6 %. According to these surveys only a minority of children with disorders is in contact with specialist services.

Prevalence of mental disorders in children: data from international studies

Disorders	Age (years)	Mean prevalence (%)	Confidence interval between studies (%)

Autism and other PPD	0-19	0.27	0.2-0.6
ADHD	5-14	2	1-5
	15-19	1	–
Obsessive-compulsive disorders (OCD)	8-12	0.15	–
	13-19	1	0.6-3
Anxiety disorders	5-19	5	2-10
Affective disorders	6-12	0.5	0-2
	13-19	3	1-5
Bulimia	17-19	1	0.5-4
Anorexia	15-19	0.18	0-1.3
Schizophrenia, bipolar disorders[1]	5-12	0.004	–
	13-14	0.1	–
	15-19	0.5	–

PPD: pervasive developmental disorders; 1 studies have often examined the prevalence of all psychoses including both bipolar disorders and schizophrenia, which is why prevalence is given for the two disorders as a whole.

Estimate of the number of children and adolescents suffering from a mental disorder in France*

	Age range					
	0-2 years	3-5 years	6-10 years	11-14 years	15-19 years	Total
Population	2,175,326	2,154,419	3,736,596	3,110,095	3,967,703	15,144,139
Autism and other PPD	2,969	5,882	10,201	8,491	10,832	38,374
ADHD		14,296	74,732	62,202	39,677	190,907
OCD			3,432	17,939	39,677	61,048
Anxiety disorders		35,740	186,830	155,505	198,385	576,459
Depression			15143	34,995	127,703	177,841
Anorexia					3,571	3,571
Bulimia					12,218	12,218
Schizo-phrenia and bipolar disorders				1,624	19,839	21,583

*: because of a significant tendency to comorbidity (one subject often suffers from several disorders simultaneously), the numbers in the individual columns cannot be added together to obtain an assessment of the global morbidity connected with these disorders

In France, epidemiological studies on mental disorders are relatively rare (one study on common disorders, one on depression, three on autism and related troubles, one on bulimia). Prevalence rates are generally of the same order of significance as international estimates: 4.4 % for depression in adolescents and 1 % for bulimia in adolescent girls. A survey performed in Chartres on more than 2,000 children aged between 6 and 11 years reports a prevalence of 5.9 % for emotional disorders and 1 % for ADHD. Finally, three studies performed in different regions indicate a prevalence for autism ranging from 0.045 % to 0.054 %. In the case of eating disorders, prevalence could be at least 5 times higher than the data given in the table suggest, as it is probable that only the pure restrictive forms of anorexia have been evaluated.

The accumulation of epidemiological data in psychiatry for about forty years has made it possible to investigate secular changes in the incidence of many mental disorders.

International data suggest an increase in depressive disorders, and also in suicides, behavioural disorders and the abuse of alcohol and psychoactive substances in the generations born after the Second World War. In the case of autism and related disorders, the absence of an epidemiological programme for surveying the population makes it impossible to investigate this issue. The prevalence of anorexia nervosa does not appear to be increasing. As regards bulimia, of very recent definition, the epidemiological database is too limited to estimate changes in its prevalence.

The number of young people in France suffering from a mental disorder can be estimated from the prevalence rates obtained in international studies (with the exception of behavioural disorders).

Among the sociodemographic determinants, gender and age exert a particular influence on the prevalence of mental disorders.

Among the individual or collective characteristics likely to exert a direct or indirect influence on a person's state of health, sociodemographic factors and patterns play a very important role.

Gender and age, which are closely related to health, have a special status in relation to mental disorders. Gender-specific hormonal mechanisms exist, which are implicated in the mechanisms of neurodevelopment. Furthermore, because of the neurobiological modifications occurring during cerebral and mental development, age cannot but appear as a determining factor.

In the child-juvenile sectors of psychiatry, boys outnumber girls until the age of 12-13. Girls then become the majority and remain the greatest consumers of care all their life. The period before and after puberty is thus a watershed in affective disorders. These disorders affect as many boys as girls before puberty, then the number of girls who express their vulnerability in this way rises to double that of boys. In the same way, eating disorders affect adolescent girls above all. The "gender and age" profile is different for schizophrenic and autistic disorders. Fifty to 60 % of schizophrenic boys are first admitted before 25 years, as opposed to 30 % of girls. The latter begin to be ill 3-4 years later on average. In the case of autistic disorders, boys are always in the majority. It appears that their overrepresentation is even higher when autism is not associated with mental handicap.

Socio-economic status, whether assessed by profession or by educational background, is frequently related to health. For a long time schizophrenia was associated with underprivileged socio-economic backgrounds, but recent studies have shown that downward social mobility was more likely to be a consequence of the illness than the reverse. In fact, before the appearance of the first signs, the scholastic achievement of schizophrenics is similar to that of their peers. After onset of the disease, downward mobility occurs rapidly. The employment status of the fathers of patients is similar to that of the general population, but the majority of children presenting with these disorders does not attain the same status. Autism, in older studies, was often associated with privileged socio-economic background, possible by virtue of the fact that parents from these backgrounds were more likely to be involved in the relevant organisations. At present, with improved screening for cases in the general population, autistic children are found in all backgrounds. Affective disorders in adolescents most often appear to be independent of their parents' socio-economic background. At the same time, the concentration difficulties, loss of interest and fatigue induced by these disorders can lead students to fail to complete their courses and thus to sign away their prospects of success in life. There does not appear to be any

preferential connection between socio-ecomomic background and eating disorders.

Most nations have experienced migratory movements of considerable significance in the 20th century. Internal migration from the countryside to towns involves a population concentration that leads to promiscuity in the use of transport and collective habitat, for example, as well as structural changes in the family. External migration brings into contact populations originating from increasingly distant geographic regions. In general pathology rates appear higher in town that in a rural environment. As regards schizophrenic subjects, studies have detected a relationship between increased rates and density of population observed both for their place of birth and their place of upbringing. Immigration is most often for economic reasons and involves healthy populations, which can, however, find themselves confronted by multiple stresses in their host country. It can also involve subjects who already suffer from disorders, which induce them to leave their community, perhaps even to look for medical care elsewhere. Studies have detected higher rates of schizophrenic and autistic disorders in the children of migrants. This could be connected with factors other than the sociodemographic. Belonging to an ethnic minority seems to be a risk factor for affective disorders only if it is accompanied by socio-economic problems. Eating disorders may be an expression of conflicts of adjustment when they tend to affect adolescent girls from traditional backgrounds.

Finally, it is important to emphasize that the evaluation of morbidity is liable to evolve because of changes in ways of living, new therapeutic discoveries and modifications in management and nosographic classifications. Today antipsychotic medication enables a certain number of patients to be followed-up on an outpatient basis, which means that they are not identified by health care institutions. Attitudes in general have changed and new generations are more willing to accept that their problem is a psychological one. The influence of the mass media on recourse to medical consultation and access to care may also be singled out.

Events in the perinatal period could increase the risk of mental disorders

The results of epidemiological studies suggest that pregnancy and birth are critical periods during which events disturbing neurodevelopment increase vulnerability to a broad spectrum of mental disorders. Several risk factors have been identified. The best-replicated data involves seasonal and geographical variation in births and in complications during pregnancy or delivery. An excessive number of winter births in persons suffering from schizophrenia has been reported in a reproducible manner by a high number of surveys performed across the world. Studies performed on persons suffering from autism suggest that the births of these subjects peak in spring or summer. The underlying mechanism remains as yet unclarified. These seasonal variations could be related to seasonal risk factors (temperature, photoperiod, seasonal virus, nutritional and/or toxic factors and possibly psychosocial factors themselves that are subject to seasonal variations). More recently, studies have shown that births in high-density urban zones could also be an independent risk factor for schizophrenia. Here again, the mechanisms underlying this association have not been identified.

Case control studies and cohort studies have shown that subjects suffering from schizophrenia are twice as likely to have been exposed to obstetric complications than subjects unaffected by these disorders. Such a history is more frequent in subjects with early onset. Even if the association is not restricted to specific complications, the most frequently observed complications are those likely to induce foetal or neonatal anoxic ischaemic lesions, such as prematurity or low birth weight. More frequent histories of obstetric complications

in the course of pregnancy or delivery have also been identified in persons suffering from affective psychotic disorders. Thus obstetric complications may induce a vulnerability to broadly defined psychotic disorders. It seems hardly likely that this association is artefactual, confounded by a third factor such as certain psychopathologic maternal characteristics that increase simultaneously and independently the risk of obstetric complications and the risk of inducing psycho-affective developmental disorders in the child. Cerebral lesions of the haemorrhagic-ischaemic type could be implicated in the determinism of this vulnerability. Data about the impact of obstetric history in other disorders (autism, ADHD, eating disorders) are more fragmented and less reproducible. It is, however, probable that exposure to obstetric complications could increase, in a non-specific manner, vulnerability to several types of mental disorder.

Other perinatal risk factors have been identified, but with a lesser degree of certainty than for seasonal variation in births or exposure to obstetric complications. The findings of studies exploring the association between intra-uterine exposure to the influenza virus and later risk of schizophrenia are contradictory. All the positive studies are based on an ecological method, where exposure was evaluated in a probabilistic manner taking into account the frequency of cases in the general population, but without any information on the individual level of exposure in subjects suffering from schizophrenia. All cohort studies, where individual exposure is documented, are negative, but their results are difficult to interpret because of the small number of subjects included. More consistent data, based upon individual serologic data, concern relations between intra-uterine exposure to the rubella virus and increased risk of schizophrenia and autism. There is a small number of studies on exposure to the rubella virus. The isolated findings reporting a relation between exposure to other infectious agents during the perinatal period (poliomyelitis virus, coxsackie B5 meningitis virus) and schizophrenia require confirmation.

A study performed on the consequences of the famine suffered in the Netherlands during the Second World War showed that subjects exposed to severe nutritional deficiencies during the first trimester of intra-uterine life presented with an increased risk of schizophrenia. An association has also been identified between exposure to famine in the second and third trimesters of intra-uterine life and increased risk of affective disorder. This study was also based on an ecological method and did not enable all potentially confounding factors to be taken into account. Relationships between nutritional deficiencies and increased vulnerability to schizophrenias and affective disorders can currently be considered merely potential. The aetiopathologic hypothesis suggests the role of nutritional deficiencies in neurodevelopmental disturbance, as in the folate deficiency model of disturbed neural tube development.

Data concerning the possible noxious role of exposure to psychoactive substances (tobacco, alcohol, cannabis, cocaine) are sparse. Some case control studies suggest that intra-uterine exposure to tobacco could increase vulnerability to ADHD. Studies exploring exposure to other illicit and licit psychoactive substances were not based on stringent methods and their results are, therefore, difficult to interpret.

Some studies have suggested that an association may exist between increased risk of schizophrenia and exposure to psychoaffective risk factors during pregnancy, such as intense stress or maternal depression. These results require confirmation by other studies.

At present it is plausible that the perinatal period is a high-risk period in the course of which exposure to factors disturbing cerebral development could increase vulnerability to mental disorders in children and adolescents. Several questions still remain unanswered: what is the role of interactions between genetic and environmental risk factors? What is the impact of secular variation in the frequency of environmental risk factors, such as obstetric

complications? What is the psychological outcome of very low birth weight infants? Some studies suggest that these infants could be at an increased risk of ADHD. Another unanswered question concerns the fact that there are significant geographical variations in the frequency of certain environmental risk factors (obstetric complications or nutritional deficiencies), while the incidence of disorders such as schizophrenia is relatively constant from one country to another.

A genetic susceptibility has been involved in the majority of mental disorders

The great majority of mental disorders in children is multifactorial in nature. The genetic factors currently implicated may, therefore, increase the risk, promote or modify the expression of a disorder, but cannot explain it completely or cause it. It is appropriate then to think in terms of genetic susceptibility, that is of genetic factors interacting with other factors, in particular environmental ones.

Few genetic studies have specifically devoted to mental disorders in children, apart from autism, ADHD and anorexia nervosa, these disorders being more typical of children and adolescents. As many mental disorders often develop later (such as schizophrenia, affective disorders) they are mainly studied in adults. Evaluations of individual risk and heritability are thus limited for child psychiatry.

Molecular genetics are currently at an intermediate phase of progress: sufficiently advanced to enable new hypotheses to be raised (both aetiological and clinical) thanks to statistics (groups of cases), but not sufficiently well researched to help with diagnosis (individual cases). Reference to genetics will thus be limited essentially to family history for some years.

One indicator of familial and genetic vulnerability is the increased risk in the relatives of an affected individual. This "relative risk", compares the risk in the relative of healthy individuals (controls) with the risk of disease in the relatives of individuals who are ill (λS). Generally, the familial history of first-degree relatives (parents, brothers and sisters, children) is used, more distant degrees of relationship being less informative. In the case of autism, for example, the risk of finding the disorder in a relative of an affected individual is 40 times higher than the same risk in the relatives of a healthy person.

Increased risk of disorder in first-degree relatives of an affected person

Disease	Risk (λS)	95 % confidence interval
Autism*	40.0	20.0-150.0
Anorexia nervosa	15.6	5.33-41.8
Schizophrenia**	10.0	?
Panic disorder**	7.41	5.65-10.32
Obsessive-compulsive disorders**	4.34	2.23-8.45
ADHD	4.12	3.34-5.09
Depression	2.04	1.37-3.02

*: an approximate calculation based on an estimate and not exclusively on data; **: calculation performed on samples which included adults

A gradient of risk exists in these diseases but, as a general rule, all these disorders have a familial component. Nevertheless, several factors play an important role in the observed differences of these relative risks. Data on heritability have several practical impact:

- identification of groups at risk. Presence of "family history" is often used to focus researches on groups at higher risk;
- if there is doubt in the diagnosis, the existence of affected first-degree family with a specific disorder may help the clinician to propose a psychiatric diagnosis
- for an affected subject, the existence of a family history gives information on type of the disorder (i.e. there is a relationship between familial history and higher severity, younger age of onset, more frequent comorbidity...).

If family studies can give an indirect estimation of the heritability, the weight of additive genetic factors (i.e. heritability in its widest sense) is better assessed through twin and adoption studies.

Heritability of mental disorders in children assessed on the basis of published studies

		Heritability (%)	
Disease	Estimated mean*	Minimum	Maximum
Autism	80	50	91
ADHD	70	50	91
Anorexia nervosa	70	50	76
Schizophrenia**	50	35	75
Panic disorder**	40	30	45
Depression	40	0 (before 3 years)	78 (adolescence)
Obsessive-compulsive disorders**	40	20	70

*: an approximate calculation based on an estimate and not exclusively on data; **: calculation performed on samples including adults

Overall, three distinct groupings emerge. In the case of autism all studies conclude that genetic factors exist, which play an essential role in the aetiology of the disorder. ADHD and anorexia nervosa have a high degree of heritability and finally, affective disorders (especially bipolar disorders) and anxiety disorders (essentially OCD and panic disorder) show a moderate degree.

Heritability testifies more to the impact of the "genetic" factor than the potential role of one candidate gene or another. Thus the heritability of anorexia nervosa is estimated to be about 70 %, but at present the most strongly implicated vulnerability allele increases the risk of anorexia nervosa by 1.8 only.

A large number of studies have attempted to identify candidate genes with, to date, disappointing results.

It is (at the most) plausible that these different candidate genes play a role in the disease in question, although the impact and specificity of these markers generally remains unclear. The most consistent results concern a polymorphism in the dopamine D4 receptor gene (a D2-like dopaminergic receptors) in which was associated with hyperactivity and with eleven positive replications (by association or linkage), and confirmed by meta-analysis..

The predictability remains moderate since the presence of the vulnerability allele of the DRD4 gene approximately doubles the risk of hyperactivity. A large number of candidate genes have been evaluated in schizophrenia and affective disorders; study findings are rarely replicated more than twice. The results of the various meta-analyses for other candidate genes are inconclusive.

Potential candidate genes

	Panic disorder*	Depression and bipolar disorders	ADHD	Anorexia nervosa	Obsessive-compulsive disorders*	Autism	Schizo-phrenia*
Candidate Genes	5-HTT, COMT, MAO-A	Many	DRD4, DAT	5HT2A	5-HTT	HRas, NF1, HLA	Many
Replicated		Yes (> 10)	Yes	Yes	Yes	No	Yes (> 10)
Candidate regions	No	Yes	No	No	No	X, 15, 7	18p, 22q11
Replicated		Yes				Yes	Yes
Screening	Underway	> 50 studies	Underway	Underway	Underway	5 studies	≥ 50 studies
Replicated		12q, 13q, 18p, 18q, 21q, Xq				7 (indirect)	5q, 6p, 8p, 10p, 13q, 22q

*: studies performed on samples including adults; 5-HTT: serotonin transporter; COMT: catechol O-methyl transferase; MAO: monoamine-oxidase; DRD4: dopamine receptor D4; DAT: dopamine transporter; HRas: *Harvey-Ras* ; NF1: *Neurofibromatosis type 1*; HLA: *Human leukocyte antigen*

Candidate regions are proposed on the basis of an excess of caryotypical abnormalities in affected subjects. Studies deal primarily with autism: karyotyping (after demethylation to facilitate identification of fragile X) should be part of the systematic examination of autistic children, especially in cases of associated mental retardation. The development of cytogenetic techniques such as FISH (fluorescence in situ hybridization) should make for easier detection of small anomalies (translocations), which have hitherto passed unnoticed.

Finally, genome screening (or genome scanning) consists of testing for the cotransmission of chromosome segments and the disease in families where several individuals are affected from one generation to another by the disease in question. This type of investigation does not presuppose that any particular region will be more specifically transmitted (non-specific probes). These studies have gained considerably in power (an increasing number of probes, increasingly high-resolution screening, increasing numbers of families). The more frequent disorders in adults (schizophrenia and affective disorders) have been the first to be analysed. Studies show that many regions are implicated, but results are rarely replicated in a comparable manner. Autism has been studied only recently, with some encouraging findings on chromosome 7: its very high heritability makes the genome scanning approach valuable, but the comparative rarity of autism necessitates large collaborative studies, which are difficult to set up. Genome scanning is underway for the other main mental disorders.

Parental psychiatric morbidity is also a risk factor, albeit non-specific, for mental disorders in children

Beyond the transmission of a certain genetic susceptibility, parental psychiatric morbidity is a non-specific risk factor for mental disorders in children. When the mother is involved, the anomalies of neurohumoral function implicated in her disease may affect foetal brain development *in utero*. Moreover, parental psychiatric disorder may be accompanied by deficient care of, and interaction with, the young child, by uninspiring parental models or even increased problems of abuse. Parental morbidity appears to have detrimental affects of a cumulative kind, since the more severe the psychopathology in the parents, the higher the apparent risk to the children of suffering from more severe and earlier-onset disorders.

The children of alcohol-dependent parents are at increased risk of externalised disorders (behavioural disorders, ADHD), and also score higher for anxiety and depression, poor self-esteem and difficulties with social interactions. As regards alcohol abuse by the mother, obviously maternal alcoholism is acknowledged among perinatal risk factors, with its attendant developmental disorders. The complete clinical picture is foetal alcohol syndrome.

The children of mothers suffering from a mental disorder (affective disorder, schizophrenia) have significantly more internalised disorders (anxiodepressive disorders) than control children or those whose mothers have other health problems. It has also been confirmed that a family history of mental disorders is frequently found in subjects affected by eating disorders and is higher in bulimics than in anorexics. The risk may be present from birth, because a schizophrenic or depressive mother, for example, cannot establish a satisfactory relationship with her child (inexpressive face, absence of smiles and dialogue, lack of physical contact), which may permanently disturb the baby's affective and cognitive development. Thus in certain child-rearing contexts in the west, maternal depression may contribute to the development of an attachment disorder, implicated itself in depressive vulnerability in the child. However, no studies find any relationship between maternal depression and insecure attachment styles. The possibility cannot be excluded that both are independent risk factors for depression in children. Attachment disorders (insecure attachment styles) have also been identified as risk factors for eating disorders. More precise studies treating the specific aspects of attachment are necessary to specify their potential aetiological role.

Parental divorce, the disappearance of a family member, parent/parent or parent/child conflicts have also been identified as risk factors for later morbidity in children.

The children of divorced or separated couples are likely to experience multiple stress factors: the parents' emotional distress, their reduced availability for the children, economic difficulties, change in social status, moving house, persistence of conflicts between the parents and the formation of new families. In the short term the parents' divorce is associated with an increased risk of general psychopathology in children, via symptoms as likely to be externalised (obvious behavioural disorders) as internalised (anxiodepressive disorders). Moreover, longitudinal studies show it is possible to identify this risk well before the parents actually separate. It seems to be connected more with parental conflicts than the divorce itself. The long-term impact of divorce on affective disorders appears to be indirect, connected with marital discord more than with the separation itself, and to occur in relation to deviant developmental pathways. If the relationship between marital conflicts and adjustment disorders in the child have been clearly demonstrated, it is important to note that most children who live through this kind of situation do not develop disorders.

According to studies the loss of the mother before the age of 11 years is associated with a significant risk of depressive disorders in adulthood (OR = 2.3 for women). The same risk probably applies to the loss of the father, but most of the available data concern female samples. Genetic factors are a source of confusion here, to the extent that the early death of the parent may also be related with a mental disorder. The death of a close relation (parent, brother, sister) is also more frequent in families of anorexic adolescents than in control families.

Parent/child relationships involving conflict (rejection or lack of care and attention on the part of the parents, lack of maternal satisfaction) have been reported in studies as being a potential source of psychological problems in children, including anxiety, depression, hyperactivity and behavioural disorders. Intrafamilial communication disorders have sometimes been considered to be determining factors in the birth of schizophrenia. But the behaviour of the parents of the schizophrenic child could be, in part at least, determined by

the communication difficulties of their child. It is difficult to determine if conflictual parent-child relationships are caused or aggravated by the disorder.

Intrafamilial abuse and violence are generally associated with a constellation of various types of family problems such as social problems (poverty, social disorganization, unemployment, death), parental psychopathology (depression, schizophrenia) or marital conflicts. The constellation of factors implicated in the emergence of physical or psychological abuse makes it difficult to assess its direct consequences on the child's emotional equilibrium. Sexual abuse in childhood is associated with an elevated risk of psychopathology in adulthood. The risk of anxiety or depressive disorders in women is twice as high, and the risk of suicide attempt twenty times as high, whatever the type of sexual abuse, compared to subjects who have not experienced sexual ill-treatment. The impact of intrafamilial violence during childhood on long-term recurrent depression is mediated by chronic dysfunction in affective relations in adulthood. The relatives of depressed-abused children have, over the whole course of their life, a nine-fold higher prevalence of depressive disorders. The authors emphasize the importance of familial depressive vulnerability, the risk probably being increased by a history of abuse. There is no specific relationship, in terms of co-occurrence, between a history of childhood sexual abuse and eating disorders.

Parenting style and parent-child interactions, in general, bring into play genetic factors (parents and children), shared environmental factors (in the parenting common to the sibship) and environmental factors that are not shared (the specific element to each child in a sibship in parent-child interactions for each child in a sibship). In internalised disorders it appears that specific interactions play an important role, although, in externalised disorders, it is the shared environmental factors in particular that are implicated.

The mechanisms of action of non-genetic familial factors remain to be investigated. Gender, individual characteristics and the macro-environment appear to play a role in the differential impact of familial risk factors.

Neurodevelopment involves gene-environment interactions

Development of the central nervous system results from the activation of genetic programmes at different ontogenic stages. Cerebral development begins with the differentiation of a neural plate at the beginning of the third week post-conception and is completed in adolescence. Neuron production continues for the whole of life. This late neuronogenesis is clearly apparent in the olfactory bulb and the dentate gyrus; its importance at the level of the associative cortex remains to be demonstrated. Environmental factors (molecular, cellular, those belonging to the organism and/or the individual) during the prenatal period, but more particularly after birth (with their potential implications for very premature infants), will modulate the expression of these genetic programmes.

The significant stages of brain development may be summarised as follows: production of neural precursors, neuronal production, neuronal migration, programmed neuronal cell death, production of neurites (axons and dendrites), elimination of surplus neurites, synaptogenesis, selective elimination and stabilisation of synapses, gliogenesis (production of astrocytes and oligodendrocytes), myelinisation and angiogenesis. It should be noted that these different developmental stages occur according to time-specific patterns particular to each cerebral structure and that, within one and the same cerebral structure, heterochrony may exist for each ontogenic episode.

Grapique 1

Chronology of the production of neuronal precursors in various neocortical layers. Heterochrony in migration between the cortical regions of areas 17 and 24 in monkeys (Rakic, 1995)
The neurons have been marked at different embryonic periods, from embryo day E40 to E165 (horizontal axis). The different layers of the cortex are indicated on the vertical axis in Roman numerals.

The processes of neuron death-survival, the pruning-maintenance of neurites and stabilisation-elimination of synapses are particularly sensitive and are controlled by environmental factors (visual, auditory, tactile and pain stimuli, nutritional factors, medicines). The organisation of the cytoarchitecture of the neuronal networks is in part independent of electrical activity and in part modulated by this electrical activity.

In order to undertake these different developmental processes, the brain has recourse to molecular tools that could play a completely different role in the function of the mature brain. The same molecule could also play varying roles from one ontogenic stage to another and antagonist molecules in the mature brain, such as glutamate and GABA (γ-aminobutyric acid), may exert a synergic action on the developing brain. In the course of cerebral ontogenesis we witness the successive superimposition of patterns of molecular progression, which control the functions of the mature brain. We witness too the orchestrated and sequential intervention by certain of these molecules in the regulation of the structuring of the adult brain (postpuberty stage). From then onwards, disturbances in any given factor during cerebral development could have three types of consequence:

- an anomaly in the establishment of the pattern of adult expression for this factor and abnormal adult functioning of the systems using this factor;
- a deviation in the developmental programmes leading, in the mature brain, to a dysfunction in systems which are then unable to maintain a functional connection with the factor that was initially disturbed;
- a combination of the two preceding phenomena.

Amongst the great molecular actors in cerebral development potentially implicated in certain psychiatric disorders, it is possible to cite the glutamatergic system and nitric oxide (NO), the aminergic systems (dopamine, serotonin, catecholamines and their receptors), the growth factors such as *Brain-derived neurotrophic factor* (BDNF), certain neuropeptides such as *Vasoactive intestinal peptide* (VIP) and the opioids. The influence of stress (via an increase of glucocorticoid production) and cytokines on several of these factors represents an acquired effect. A disturbance in these mechanisms may occur at any stage of cerebral development. It is clear that the functional consequences will depend on the developmental stage involved.

Knowledge of neurodevelopmental processes has benefited greatly from major progress in cellular and molecular biology. The animal model descriptions of developmental anomalies by animal models has seen an extraordinary expansion in the last twenty years. However, the emergence of specific animal models for psychiatric disorders has remained relatively anecdotal, probably because it is difficult to correlate the manifestations observed in laboratory animals with the clinical signs presented by patients suffering from psychiatric diseases. Finally, few neuropathologic studies (and in particular those based on the use of modern molecular tools) are available to child psychiatry.

Neurobiological disturbances are observed in certain mental disorders

Mental disorders in children and adolescents correspond to the occurrence of a pathologic process in the course of a neurodevelopmental phase (embryonic or postnatal), during which

neuronal plasticity is particularly important. The modifications induced then become part of this developmental process and certain environmental factors can leave a "neurobiological" trace. It is difficult to determine, *a posteriori*, whether the origin of such traces is acquired or constitutional. Accordingly neurobiological or neuropathologic anomalies correspond to "scars", - of the anomaly itself or of its direct or indirect consequences (in particular when a critical period is over-run, thus making maturation impossible) or of an overcorrection process (aberrant reinnervation, for example).

The neurobiological approach involves the study of neuronal modifications and of neurotransmissions (monoamines, excitatory amino acids, peptide and trophic factors). It is in fact indistinguishable from the pharmacological approach (behaviour modifiers, receptor studies, dynamic provocation tests), from the neuropathologic approach (modifications visible on histological tissue pieces *postmortem*) and from the endocrinological approach (regulation of peptide factors).

The mental disorders occurring in children are divided into two types. It is possible to distinguish adult disorders, which begin in childhood, such as affective disorders, schizophrenia or anxiety disorders. This raises the question of the specificity of the disease as observed in children relative to adults: is it a case of the same disorder expressed differently according to the age of onset or is it a disorder connected with different pathophysiological processes? The second type of mental disorder includes more specific disorders in the child such as pervasive developmental disorders (autism) and ADHD. In aetiological terms it is easier to recognise an "innate" endogenous vulnerability in these latter disorders, where the impact of genetic factors is considerable. However, anxiodepressive disorders appear to fit more readily into a model where environmental factors play a role in revealing a particular genetic background.

To date there is no mental disorder in children the pathophysiological mechanisms of which are clearly elucidated. Moreover, in disorders individualised by conventional nosography existing data show a certain overlap in the anatomical locations of the anomalies observed or systems of neurotransmission. Thus, similar anomalies of the hippocampus have been noted for depression, schizophrenia and post-traumatic stress disorder. In addition, abnormalities of blood serotonin have been found in autistic disorder and depression, and also in schizophrenia, obsessive-compulsive disorder, anxiety and eating disorders. These abnormalities may be the causal process of the disorders, or they may result from the aetiological abnormality itself.

The evolution of concepts concerning psychiatric illnesses in children and adolescents is increasingly directed towards recognition that pathophysiological anomalies play a direct role in the developmental process. Concomitantly, a flaw in adaptation and/or postnatal neuronal plasticity in response to a pathophysiological process (pubertal maturation) or an environmental stress is now studied as a potential mechanism explaining certain mental disorders. It is from this perspective that the study of modifications in certain proteins involved in neuronal differentiation and survival (BDNF, *brain-derived neurotrophic factor,* or other cytokines), in intercellular recognition (N-CAM, reelin protein) or in the maintenance of the integrity of the cytoskeleton (MAP, *microtubule associated protein*) is relevant. We now recognise, on account of these different proteins, or related proteins, a role for the process of neuronal plasticity even beyond the developmental period.

The model of acquired vulnerability during the postnatal period is based on the importance of functional and/or structural changes connected with postnatal plasticity, which is a necessary condition for a subject's satisfactory adaptation to his environment. The animal model of early stress (maternal deprivation) is particularly valuable for exploring anxiety or depressive disorders. Study of post-traumatic stress disorder in humans or animals has

shown the involvement of regulation of the hypothalamic-corticotropic axis or the induction of structural anomalies by stress (modification of the dendritic tree, even of the number of cells by neurotoxicity *via* the glutamatergic system).

Mental disorders in children and adolescents, like those in adults, appear then to be, in the main, multifactorial and possibly heterogeneous in their aetiological mechanisms. The vulnerability model whereby certain environmental factors interact with a genetically predisposed terrain could account for several mental disorders, in particular anxiety and depressive disorders or certain psychotic disorders. These studies have shown in particular the involvement of hormonal factors and peptide factors with a trophic role in neuronal or synaptic plasticity and their effectiveness with regard to neurotransmission. A study of the patterns of expression of these various peptides in histological material *postmortem*, and in animal models should, in particular, provide important information for the understanding of the pathophysiological mechanisms of mental disorders.

The cognitive approach enables us to break down the mechanisms of normal or pathologic mental functioning

Cognitive psychology covers the experimental study of normal or pathologic mental functioning and its development. The term cognitive designates here all the mechanisms involved in mental functions, conscious or not, (the mechanisms of perception, attention, decision, various sorts of memory, imagination, dreaming, language, of the initiation and planning of action). It also embraces the emotional aspects of behaviours and mental states. This scientific field has taken its place in the context of the cognitive neurosciences, where mental functioning meets its neurobiological foundations.

As with every approach to the biological systems, an understanding of pathologic phenomena requires some exchange between the study of the normal and that of the pathologic. The general methodology is close to that used to understand vital functions and consists of breaking down mental functions into mechanisms for the transformation of information, of identifying the cerebral regions, neuronal networks and neurotransmitters, as well as the neuromodulators involved. This "dissection" of the functions is made possible by very precise mental tasks. Thus the study of the different components of attention in adults and normal children permits us to begin to identify the mechanisms that are disturbed and those preserved from damage in the different syndromes.

In adults, studies of mental functioning in the case of focal cerebral lesions show that different mental abilities, which appear *a priori* to be intimately connected, are in fact dissociated. This leads to individualisation of different functional modules. A "module" corresponds to a large network of neurons crossing many primary, secondary or associative cortical regions. The components of this network specialise in processing different types of information: some are poorly integrated, others highly integrated. The module "recognition of faces" for example in adults comprises a network, certain components of which are brought into play in elementary visual activities (representation of curves, horizontal lines, weak or strong contrasts) and complex activities (representation of shapes); one part alone of this network is brought to bear essentially or even exclusively in the processing of faces. Disturbance of one module may thus have crucial effects but leave other, proximal functions intact. Lesions may thus lead to severe disorders in the perceptive recognition of objects while sparing the perception of faces and mental representations of these objects. Conversely the loss of the ability to recognise familiar faces and to learn to recognise new faces (prosopagnosia) may coexist with a preserved capacity to recognise the facial expression of

emotions. The retention of recognition of the identity of familiar faces may co-exist with the loss of the feeling of familiarity with the persons recognised. In the same way, reading disorders originating in "phonological dyslexia" leave intact the manipulation of mathematical symbols and arithmetic.

Among the data obtained in adults that are pertinent in helping to understand certain mental syndromes in children, the various functions of the prefrontal cortex and the disorders associated with its lesions have played an important role. In adults the prefrontal cortex essentially performs a filtering and selection task. It focuses the excitation and inhibition of the networks involved in the emotions and the networks of the posterior cortices, which are involved in the processing of information about the environment and in the production of explicit or implicit, real or imaginary, mental representations of the world. Our knowledge of the development of these functions in children is poor, all the more so since a heterochrony of maturation of the cortical networks exists. For example the posterior cortices mature more rapidly than the prefrontal cortex. But the different networks of the prefrontal cortex and their connections with various networks of the posterior cortices mature at different periods of development. As the networks of the prefrontal cortex do not all develop at the same rate, it is understood that certain regulatory and executive mechanisms of the processing of information and mental representations may develop normally while others function abnormally.

The question arose whether mental development consisted in the evolution, with age, of various modules independently of each other, with the corollary, that every mental disorder could be characterised by a deficit in the specific modules. It is known, for example, that speech disorders exist without other cognitive disorders being present. A study of the capacity to "understand the mental states of other people" (or theory of mind), undertaken in healthy young children, has thus made it possible to propose that infantile autism consists of a deficit specifically and essentially affecting this representational function. At the same time, several studies performed in autistic children reveal that this ability varies. In addition, certain data suggest the existence of much more elementary deficits in the sensory mechanisms (perception of movement, face recognition) and of anomalies of neurophysiological functioning that are as yet poorly identified. Behavioural disorders observed in the autistic child in his complex mental functions could thus be the consequence of early disturbances in the elementary mechanisms for dealing with information. Given the cascade of mechanisms involved in the development of cerebral organisation in the course of its development, the idea that an anomaly of cerebral development intervening very early in the construction of the brain (during the perinatal period) could affect exclusively the development of one mental "module" alone, at a very high level, is not a very plausible hypothesis. Nevertheless, there is a certain independence between the development of different mental functions. It is this relative independence which allows targeted re-education procedures to be developed in certain syndromes.

The resemblance between two behaviours (or abilities) and the chronological precedence of the one over the other in terms of development are not evidence that the first behaviour is an intermediary phase necessary for the appearance of the second. Thus walking on four feet is not a necessary step to walking upright. The existence of perceptual abilities that permit understanding of physical phenomena in the infant before the age of 5 shows that it is not manipulation of objects alone that allows the child to discover their properties. Children with peripheral motor disorders (caused by poliomyelitis for example) can develop normal visuospatial abilities (to put it another way, the teaching role of the manipulatible environment probably belongs among the preliminary organisers of neuroperception). In infants production of the sounds of language follows their perceptual organisation, contrary to what has long been believed. This does not, however, mean that the development of motor

activity does not modify mental, spatial or vocal representations and actions. It may well be, for example, that significant visuospatial disorders observed in children presenting co-ordinated developmental deficits result, in part, from disorders in motor co-ordination, unless they both have the same pathologic cause. The same applies in other sectors. The reactivity of the neonate to the emotional expressions of the adult does not imply that the latter are the exclusive determinant of the child's later socio-affective behaviours.

Lack of understanding of the "precursors" of a behaviour makes it difficult to identify the beginnings of a dysfunction in the course of development. An apparent absence of behavioural beginnings may signify either that none exist, or that they are not found in the relevant pertinent sector of abilities. So the signs of autism in children before the age of 18 months have not yet been identified. In the same way, identification of attention disorders with hyperactivity before the age of 4 is difficult.

Functional cerebral imaging enables us to follow the changes with age in regional metabolic activities or the evolution of electrophysiological signals in the course of a cognitive task (cognitive evoked potentials). Study results as a whole suggest on the one hand, that cortical maturation proceeds by successive waves that affect networks involving several cortices, and not region by region, and on the other hand, that the *patterns* of neuronal activation observed in the course of a task are, in children, only partially identical to those in adults. Studying the cerebral correlates of the mental activities revealed by "marker" tasks makes it possible to detect, in the healthy subject, the neuronal networks involved in this mental activity or to locate, in the sequence of events processing the signal, the precise moment where the anomaly of function occurred. Thus it has been shown that reading words is associated with an abnormal cortical activity in dyslexics. The neuronal network in the left temoroparietal and occipital temporal regions are much less activated than their homologues on the right in dyslexics, while in normal readers they are more activated. In the same way, the recording of evoked potentials in schizophrenic adolescents in the course of a "marker" task reveals abnormalities in certain electrophysiological components.

Functional cerebral imaging gives us information on the cerebral correlates of a mental anomaly at the age of examination, but not on the processes by which the pathology developed. For example, observation of a hypofusion in a given cortical zone enables us to detect neuronal networks functioning in an abnormal fashion, but not to determine at which stage of their development these networks became abnormal. In certain cases, however, temporal indicators may be present, as for example, when anomalies of neuron migration in a precise region are observed.

One of the main questions about the child's mental development concerns the long-term effects of the environment on the brain and the organisation of its functions. At present, we are obliged to infer the effects of the socioaffective environment from what is known about the effects of the physical and "cognitive" nature of the environment. The effects of the socioaffective characteristics of the environment are difficult to study, control and manipulate in humans as in other species. A certain number of characteristics of the environment of light and sound, universally encountered and absent only exceptionally, are necessary for the development and organisation of the primary cortices, of vision, hearing, etc. The period for which these effects can be exerted and the period during which their absence has few harmful effects are still poorly understood: a certain number of growth factors play a role in the temporary maintenance of plasticity. Modifications of dendritic arborisations and synaptic density are observed in accordance with the richness or poverty of the environment. The effect of early experiences on cognitive abilities as on cortical organisation has been demonstrated in certain ability sectors: acquisition of the mother tongue diminishes the ability to differentiate foreign sounds (a reduction is observed

towards the age of 10 months in the ability to discriminate sounds foreign to the language of the child's environment). A peripheral deficit in the visual pathways may have significant long-term consequences. Sometimes characteristics resembling certain autistic traits are found in children affected by a congenital peripheral blindness. In addition, children undergoing surgery at about 4 years of age for an opaque bilateral cataract still present, in adolescence, a particular mode of processing visual information, which is a distinctive feature attributed to the deprivation of vision during the first months of life. In other cases, as a function of age, of the state of maturation of the cortex, and of the duration of the interaction considered, sensory deprivation or harmful stimulation may have no effects, or only short-term effects (in rats for example the effects on the development of the young of episodes of pronounced stress in the pregnant mother are less permanent than the effects of slight but repeated stress).

Apart from the relatively non-specific effects of stress, the specific effects of abnormal social or affective environments have been subject to little systematic study. It is advisable to distinguish, among the potential effects of abnormal affective-cognitive environments, the substantial effects that may modify cerebral development in a relatively non-specific way. For example, it appears, in particular, that somaesthetic stimulations trigger - alongside specific learning phenomena in the course of relational transactions - more or less aspecific mechanisms, which may play a trophic or global reinforcing role. A substantial deprivation of stimulation risks excessive reduction of these non-specific mechanisms in too great a way. Painful abuse or shaking, which triggers cascades of deleterious changes to the nervous system, is another source of substantial noxious effects on cerebral development. There may also be more subtle, more specific effects, which direct and specify the functioning of the neuronal networks, by entirely normal mechanisms, and contribute to the development of varied cultural or familial affective attitudes and habits, whether harmful or not. It has not yet been demonstrated that socially acceptable adult attitudes are enough to provoke in children developmental effects as devastating and specific as those found in the syndromes discussed in this expert panel report.

Learning difficulties may express a dysfunction of cognitive development

Learning delays and disorders may appear in isolation, that is to say, independent of all other disorders of mental activity and without identified neuro-anatomical correlates (early cerebral lesions, cerebral motor weakness, epilepsy), or make up a complex profile of disorders (infantile autism, psychosis, attention disorders). Such learning disabilities have effects on the educational, social and affective outcome of children and adolescents.

The question of learning delays and disorders may be addressed by recourse to cognitive models of development, which aim to describe the functional architecture of the different information processing systems implanted in a brain during development, to clarify the nature of the representations on which these processings are performed and to specify the rapid information processing accomplished by the different components involved in these architectures.

The cognitive approach proposes to "locate" functional lesions in the course of information processing in order to account for the nature of the deficit, that an observation of its superficial manifestations does not enable us to discover. It describes information processing systems in the context of which mental states are to be explained. According to this approach specific dysfunction is caused by genetic and environmental factors and disturbs cerebral development. There is a connection between progress in the understanding of normal cerebral development and progress in the understanding of disorders relating to

development. If mental functions have often been considered to be modular, it is known that different modules react differently to disturbances connected with development.

Do the characteristics of specific disorders of language development result from a unique deficit or a combination of deficits on several levels of analysis and processing (poor phonological representation in vocabulary, inability to programme speech at its expression and/or lack of co-ordination of speech motor control)? In adults with an acquired disorder, these levels may have deteriorated differently, but it is not certain that the effect of poor functioning at any one of these levels (for example, the level of temporal auditory processing, of the phonological system and analysis of linguistic representations, particularly lexicogrammatical ones) is sufficiently well developed in children for poor functioning to manifest. Two types of dyslexias correspond to a specific reading stage: developmental dyslexia is connected with an arrested logographic phase and thus the non-mastery of the phonological phase, and developmental dysorthography is connected with non-mastery of the orthographical phase. Three types of specific calculation disorders exist, a defect in the numerical transcoding of the names of numbers heard into letters, a deficit in the construction of arithmetic acts and a procedural memory deficit (reasoning memory).

Attention deficits in children and adolescents and the distinctive characteristics of memory identified using functional cerebral imaging techniques permit us to think in terms not only of the existence of a disorder of the executive functions but also of associated behavioural disorders. By bringing to light in this way the mental processes which underlie behaviours, the cognitive approach to development may help us refine diagnostic and prognostic strategies and to define screening activities and early interventions in specific retardations and learning difficulties.

Cerebral morphologic and functional anomalies are associated with the cognitive dysfunctions seen in certain mental disorders.

Brain imaging in mental disorders is a relatively new field. Its development is a corollary of the progress in medical imaging- in image acquisition methods as well as in image analysis - made during the last ten years. There has been uninterrupted progress in accessible spatial and temporal resolution, which is currently in the order of a millimetre for morphological measurements and of a second for functional measurements. Under experimental conditions the technical constraints of the latter require immobility and mental activity.

Nuclear magnetic resonance imaging (NMRI) should be used for research on brain morphology and function in children and adolescents. Indeed, the quality of the measurements performed without the necessity for contrast medium and ionising radiation is peculiar to this technique. The feasibility of examining cerebral function with MRI increases with age and becomes easier to interpret in adolescence. Alongside the straightforward inspection of images by an examiner, computerised analysis methods make possible the detection and quantification, without any intervention from subjective judgement, of changes in morphology and function in each of the elemental "volumes", known as voxels, the sum of which constitutes the image. This method of objective analysis is currently used in research but, as it becomes applicable on the individual level, it could gradually become a part of routine diagnosis.

The usefulness of imaging cerebral morphology is demonstrated in the differential diagnosis of neurological diseases that are revealed by psychiatric symptoms. Thus, in adults, it has been possible to detect about 17 % of neurological lesions in an examination of this type, performed at the request of a psychiatrist suspecting a neurological disease, in the absence of

any syndrome composed of clinical signs. In the absence of retrospective studies, the relevant proportion is not well documented for children.

The indications for morphological imaging in child and adolescent psychiatry are currently movement disorders of unknown aetiology, severe affective disorders and psychotic disorders that do not respond to conventional treatments, anorexia nervosa (to eliminate pituitary disease) and confusional states of unknown origin. Cerebral morphological imaging could contribute to aetiological diagnosis of mental retardation and play a role in the overall assessment of addictions (alcoholism and drug addictions).

The other applications of cerebral imaging in child and adolescent psychiatry pertain to the field of research. The occurrence of mental disorders in developing subjects makes the acquisition of information on normal regional cerebral maturation indispensable. This has been studied in normal children and adolescents by brain imaging methods. Variations in regional cerebral activity measured by glucose consumption or blood flow have been demonstrated. These variations appear to relate to the stages of cerebral development. Thus, glucose consumption, which measures regional energetic activity, is very low at birth, similar to that of the adult when approaching 2 years, and twice as high at the age of 3-4 years. It remains stable up to the age of 9 years, then reduces progressively to reach adult values in late adolescence. In children, increased activity in the different regions of the brain appears to correspond to the acquisition of cognitive abilities, in accord with what is known about functional specialisation in these regions. In the same way, regional morphological variation is first described, in particular during adolescence, when regional reductions in the size of the frontal, parietal or sub-cortical cerebral regions are contemporary with the cognitive acquisitions belonging to this period. It is not surprising, therefore, that brain imaging reveals changes in cerebral anatomy in the course of neurodevelopmental disorders that lead to mental retardation. Thus 25 % of the causes of mental retardation which interfere with cerebral development are accompanied by detectable organic deterioration. But, in the absence of databases of images of cerebral anatomy, which would make statistical studies possible, it is still too early to judge the diagnostic specificity of regional anomalies.

In adolescents and young adults suffering from a learning difficulty involving reading, phonological dyslexia, the shape of a brain region involved in the processing of words (*planum temporale*) appears on anatomical MRI scans to be abnormally symmetrical. Further research is necessary in order to estimate the value of this kind of observation in the detection of these disorders.

In conditions that are conventionally the concern of child psychiatry, cerebral imaging methods transform our understanding of brain involvement in mental disorders. Thus, childhood autism appears to be associated with anomalies of cerebral functioning. Reductions in the size of the cerebellum have been reported in several studies, as well as hypofunction of the temporal regions involved in the perception of auditory integration.

Recent data from imaging research emphasize the involvement of the encephalon in other mental disorders. In early-onset schizophrenia, morphological anomalies have been demonstrated by statistical image analysis. In particular, it is the regions of grey matter known as “limbic” whose size appears to be reduced. A reduction in volume of grey matter has also been reported in the frontal regions. Functional anomalies have been consistently reported in the anterior and posterior heteromodal associative cortices involved in the higher integrative functions like attention, language, working memory and executive functions. The development of the heteromodal cortex is later than that of the other cerebral regions and could be completed only in adolescence or in the young adult. The best hypothesis to explain cerebral changes distributed in this way (between the limbic system and the heteromodal cortex) would have it that anomalies of cerebral development are produced in two “waves”.

The first would be an early wave, during pregnancy, the neonatal period or early childhood, which could concern the limbic regions. The second wave would occur later, during adolescence, and would be connected with anatomo-functional deterioration of the heteromodal associative cortex. This neurodevelopmental hypothesis of schizophrenia, originating from recent data supplied by cerebral imaging, does not prejudge the respective influence of genetic or environmental factors. The information supplied by brain imaging in schizophrenia emphasizes that the inference of causality in terms of "disease" is not necessarily the main aim of research in functional imaging. It is less important to know if an anomaly in such or such a group of regions "explains schizophrenia" than to describe the regions whose activity modulates an elementary cognitive function, deterioration of which is connected with the schizophrenic pathology. Certain therapeutic research is moving towards the modification of the activity of these structures. It could be a matter of evaluating pharmacological effects and/or the effects of certain forms of psychotherapy and also those of new methods such as transcranial magnetic stimulation, which is beginning to be studied in schizophrenia in adults, with promising results.

In obsessive-compulsive disorder reductions in the size of regions situated at the centre of the brain (putamen, thalamus) have been documented. When obsessive disorders have an infantile/juvenile onset, it is probable that the repetitive, stereotypical and chronic character of the obsessions and compulsions is connected with anomalies in the development of the regions involved in controlling selection of behavioural responses, such as the frontal-basal and cingular cortex, and that their functional relations with the central grey nuclei have deteriorated. Analogous mechanisms are also suspected in Tourette's syndrome.

In ADHD in children and adolescents deterioration in the incorporation of a catecholamine precursor, 18F-dopa, has been reported in the brainstem and mediofrontal regions during studies with positron emission tomography. This decrease in the metabolism of a radioligand assessing dopaminergic function can be judged in relation to the fact that a relative improvement in this disorder can be achieved by stimulants of the dopaminergic system.

In the course of eating disorders, in particular in anorexia nervosa, "pseudo-atrophy" can be detected in images of cerebral anatomy. Initially considered as reversible on the correction of nutritional disorders, more recent imaging methods of grey matter do not permit us to be so positive. It is possible that some anorectic subjects do not have their grey matter restored *ad integrum*, even after reverting to normal diet and weight.

Research in functional brain imaging aiming to map the regions involved in cognitive or emotional functions are currently being carried out in adults in general without psychiatric disease. However, a number of results may have theoretical implications relevant to child psychiatry. Thus, certain groups of cerebral regions, the frontal, cingular complexes in particular, are involved in the functions controlling strategies for carrying out cognitive tasks (what is known as executive functions) and in the integration of emotions. As a result, it is possible that the distinctive nature of the affective conditions for learning or identification given by the parents (absence of help in resolving emotional conflicts, poor protection against feelings of distress, or contradictions between emotional behaviours) may have consequences for the development of the cerebral regions involved in the cognitive functions. Thus, brain imaging research suggests that cerebral development in the affective domain could be intimately connected with the quality of acquisition of the cognitive abilities. As an approach to mental disorders in children, functional brain imaging appears to be in transition. Resolution of this type of hypothesis would allow us to build bridges between the old theoretical approaches and the more scientific approaches of psychopathology. Confirmation of this type of hypothesis requires study of the regulation of

interactions between the different cerebral regions.

The data already obtained illustrate the potential of brain imaging in the field of diagnosis assistance, pathophysiological research, and even therapeutic evaluation in the context of mental disorders in children.

How do we attempt early detection of autism during the first two years of life?

Autism involves qualitative impairments in the three major spheres of development: the development of language and communication, the development of social relationships and the development of play and interests. The qualitative nature of developmental abnormalities in autism is emphasized because it is important to differentiate between the concepts of retardation and deviance in order to characterise autistic development. The development of important functions may be marked by a more or less severe retardation, but what actually defines autism is the concept of deviant development: capabilities are not used in a functional manner, regardless of the level to which they are developed in children at any given time and after taking any degree of retardation into account. Thus the delay in the development of spoken language is the rule in the young autistic child, although it is also observed in a wide range of developmental disorders, which are not autistic. The autistic child, however, does not compensate for its lack of language by any of the alternative modes of communication children use to communicate before language is established. Thus, the autistic child does not use gestures to make himself understood, does not point at what he is interested in to show it to his parents, and his communication strategies with those around him are often difficult to understand. In short, the disorder affects all his communication functions, not only language. In other words, the absolute level of language development counts less in the diagnosis of autism than the child's profound difficulties in employing the tools of communication to enable him to communicate with others. Social interaction in autistics is adversely affected and profoundly so. Symptoms range from impairment in the use of the non-verbal behaviours that regulate social interaction, withdrawal into the self, a marked lack of affection for others or paradoxical emotions, to more subtle abnormalities including lasting difficulties in initiating and maintaining interpersonal relationships and friendships.

In the past, children suffering from autistic syndromes were not often diagnosed until they started primary school. At present, in most countries, the mean age at which children are now evaluated and diagnosed has reduced and is around 3-4 years. It is extremely difficult to make a diagnosis of autism in very young children (less than 1 year), because their behavioural repertoire is too restricted to identify reliably the symptoms typical of the autistic syndrome. Abnormalities in communication and language are much more difficult to detect in children at the preverbal age. The same applies to abnormalities in social interaction, which tend to be more striking when the child begins to attend a creche or day nursery. However, most parents begin to worry about their child's development before his second birthday, typically around 15–18 months, especially if they already have an older child and are thus more capable of an early identification of the initial symptoms of abnormal development. Frequently some time elapses between initial parental concerns and diagnostic confirmation.

In the case of autism and pervasive developmental disorders (PDD) it is possible to think in terms of three levels of screening, each of which requires different strategies and tools. The first level is that of systematic screening in the general population. The children participating

in the screening will not have shown particular developmental difficulties nor will their parents or carers have any special concerns. The second level concerns early detection of autism in children for whom developmental problems of differing nature and severity have already been identified. This level of screening corresponds to consultations with specialists in developmental disorders for example (orthophonists, neurologists, psychometricians, psychologists, psychiatrists), who could benefit from instruments separating autistic developmental disorders from other kinds (specific language difficulties for example). Finally, the third level represents evaluation and diagnostic activities by teams specialising in the diagnosis of PDD, who confirm or exclude the presence of a disorder in the child presenting with strong grounds for suspecting a disorder of this kind. The distinction between the three levels is to some extent arbitrary and reflects health service organisation and consultation procedures rather than the specific characteristics of PDD. The mission of the health care system is to ensure that a child suspected of autism can move rapidly from one level to another and that, at every stage of screening, sufficient expertise is available to answer the questions raised by a case of atypical development. Timely diagnosis is important for children with a PDD as well as for their parents, and allows initial treatment to be put into place. The importance of early diagnosis and initial interventions has been emphasized by recent studies showing substantial gains in terms of cognitive and language development when educational programmes are sufficiently intense (> 20 hours/week) and commenced early.

It is advisable to develop the training of primary care physicians in screening for early manifestations of PDD and to enrich the contents of systematic medical examinations by activities and questions which aim to detect them. Analogous recommendations have been recently made in Great Britain and North America. Standard questions in the three developmental spheres where the symptoms of PDD manifest could be introduced into the systematic medical examination of children under 3 years of age. The absolute presence of warning signs, even if they are not exclusively specific to PDD, should trigger a second examination.

Absolute warning signs of pervasive developmental disorders

- No babbling at 12 months
- No gestures (pointing, waving goodbye with the hand) at 12 months
- No words at 16 months
- No spontaneous combinations of two words (not just echolalia) at 24 months
- Any loss of ability whatsoever (language or social) at any age

CHAT (Checklist for autistic toddler) is the first instrument to be developed for the purposes of the systematic screening of children of 18 months in the general population in Great Britain. It includes questions on social play, interest in other children, symbolic play, protodeclarative pointing and joint attention. It also contains control questions (for example on physical and bodily play) which should not be affected in autism, and questions enabling the presence of an associated mental or motor retardation to be listed. The M-CHAT (Modified-checklist for autism in toddlers) is an extension of CHAT oriented towards children of 24 months. It possesses better metrological qualities than CHAT, is based only on the parent and does not require direct participation by, or training for, the professionals involved. The costs of using it are thus reduced. Studies are, nevertheless, still needed to evaluate fully its properties.

The development of screening instruments responds to the need, recognised in all countries, to improve identification and detection of PDD at an early age. The important question, for

example, is whether it is possible to screen children before their first birthday. A CHAT equivalent that could be used in the first year is currently being developed. In the meantime, the existing instruments supply a conceptual and practical guide for non-specialised professionals, which they can incorporate to advantage into the study of the developmental problems that are brought to their attention.

How can ADHD be identified in the pre-school period?

ADHD in children is one of the disorders where early screening may enable therapeutic strategies to be set up, whose efficacy has been established in both the short and medium term. Hyperactivity is one of the most frequent causes of consultation for behavioural disorders in children. According to the classification used it is called an "attention-deficit/hyperactivity disorder" (DSM-IV), "hyperkinesia" (ICD-10) and "psychomotor instability" (French classification of mental disorders in children and adolescents). The first two classifications have been used in the numerous studies that make up the main body of the currently available international literature.

In these two classifications, ADHD is defined on the basis of clearly identifiable and reproducible criteria, permitting identification of the syndrome and a high quality of interjudge reliability. Three principal dimensions to the syndrome are recognised. Motor hyperactivity is made up of an incessant agitation, an inability to remain still when conditions demand it (in school in particular) and disorganised and ineffective activity. Attention deficit is characterised by the inability to complete a task, frequency of memory lapses, distractibility and refusal or avoidance of tasks demanding sustained attention. The final element is impulsivity, defined by difficulty in waiting, the need to act and a tendency to interrupt the activities of others. The main characteristic of the syndrome concerns the effects of these various manifestations of the disorder on the child's functioning in various situations (school, domestic activities, leisure activities). Clinical presentations can be differentiated according to the main signs and symptoms. There are forms where hyperactivity predominates, forms where inattention dominates and mixed forms.

In epidemiological terms, the mixed forms are the most frequent, more frequent than those marked mainly by motor hyperactivity. Questions remain, however, regarding the chronology and recognition of manifestations. Thus, inattention could be more difficult to identify or be identified later, because it is less easily observed in the absence of restrictions, especially those connected with education.

The mean age of diagnosis is generally 7 years, but studies suggest an early onset of the disorder, which could, in certain cases, be apparent from the age of 3 onwards. The first manifestations are generally behavioural, and are the agitation and intolerance of frustration type. However, recognition of attention disorders is difficult in young children. Furthermore, there is a time lapse between the appearance of the first clinical manifestations and their effects on the children's functioning, the latter becoming evident later.

Epidemiological data suggest a pronounced male predominance in the disorder. These data are currently being modified by the recognition of certain forms in girls, which could be more strongly marked by attention problems, and thus less readily identified. Furthermore, the forms in girls would be less often associated with other behavioural problems such as oppositional defiant disorders or behavioural disorders.

Other forms have been described which may be distinguishable from the primary picture. Certain forms, associated with somatic conditions, with clinical pictures of behavioural disorders close to ADHD, have been described in progressive neurological disorders and in

children with significant neonatal histories (neonatal distress, low birthweight). Forms combining manifestations of hyperactivity with developmental disorders have also been observed. Certain authors distinguish a disorder where a joint deficit in attention, motor control and perception is found. In clinical terms, these forms are characterised by the presence of minor neurological symptoms, disorders of motor co-ordination and visuospatial difficulties. Their individualisation is still under discussion at present and differences between them remain to be established, especially in terms of therapeutic response.

One of the important characteristics of ADHD is the frequency with which it is combined with other disorders (comorbidity), estimated to be present in between 50 % and 75 % of cases. The most frequent comorbidities are the other behavioural disorders (oppositional defiant disorders, most often characterised by systematic oppositional behaviours in the family environment, and behavioural disorders, which combine aggression and antisocial behaviours). The coexistence of emotional disorders (anxiety and/or depressive disorders) is equally high in 20 % to 40 % of cases. Finally, there are other associations to report. One, very frequent, association is with learning difficulties (especially of written language). The other rarer association is with motor and/or vocal tics. Both pose real therapeutic problems.

These data as a whole suggest that diagnosis of ADHD can be made only after a careful evaluation. The diagnostic procedure combines discussion with the parents, observation of the child and assessments made by as many people as possible who are involved with the child, starting with information from his school in particular. This predominantly clinical procedure is effectively undertaken by using evaluation scales which make it possible to quantify the main manifestations of the disorder that can be observed in various situations (family home, school). Validated tools, which permit such an evaluation, are currently available in French. The best known is the Conners' rating scale of which three versions are available (parents, teachers, short form). A behavioural inventory is also widely used, the *Children behavior checklist*. Other scales exist, but have been subject to fewer validity studies. The use of cognitive attention tests remains limited in current practice to forms where attention deficit predominates, accompanied by significant learning difficulty.

All in all, ADHD is a disabling disorder in children. Its onset is often early, but diagnosis cannot be made until all its clinical manifestations have been observed and until its effects are significant. The latter depends on the child's environment and the demands that he may face. This explains how starting school often reveals the disorder. The most frequently asked question is whether the manifestations observed are normal or not. The answer can come only from a careful, standardised assessment of the child. The early onset and the fact that the reasons for alert are at times non-specific in nature justify providing general practitioners and teachers with information, if not training, in the realities of this childhood disorder, by reason of their potential role in screening in particular.

How can the delay be reduced between the appearance of the first symptoms of obsessive-compulsive disorder and its diagnosis?

Obsessive-compulsive disorder (OCD) is by no means a rare disease in children and adolescents. Its mean age of onset is 10 years and its gender ratio is balanced. OCD has only recently been distinguished as a pathologic entity in children, despite old descriptions of it. It is characterised by the fact that it handicaps the child's functioning and by the significant delay between the appearance of the initial symptoms and diagnosis. The source of the

delay in diagnosis is, on the one hand, the difficulty in distinguishing the obsessive-compulsive manifestations of the disorder from the rituals frequently observed during a

child's development and, on the other hand, the frequently non-specific nature of the warning manifestations in children. These two aspects justify a particularly rigorous diagnostic approach.

OCD in children has many clinical features similar to those of the form encountered in adults. As regards diagnosis, the criteria proposed by DSM-IV are acknowledged to operate in these age ranges. They require the presence of obsessions and/or compulsions almost every day, over a period of at least two weeks. The symptoms experienced by the subject, like the products of his own thoughts, are repetitive, unpleasant and recognised as excessive or absurd. They are associated with the subject's efforts at resistance and involve a momentary reduction in anxiety. These manifestations cause significant distress and/or are time-consuming (take more than one hour a day), significantly interfere with the patient's functioning. DSM-IV emphasizes that, in children, recognition of the morbid nature of these thoughts is not necessary for diagnosis.

Mixed forms, obsessive and compulsive, are the most frequent in children. Compulsive washing, checking and repetition are most frequently found. As regards obsessions, they mainly concern fear of contamination or aggression, and often have a sexual or religious theme.

The comorbidity of OCD in children is substantial, involving 60 % to 75 % of cases. The most frequently associated disorders are other emotional disorders, anxiety disorders and depressive disorders. Other pathologies on the obsessive-compulsive spectrum such as trichotillamania (hair pulling) or onychophagia (gnawing the nails) may also be found in children. The presence of motor tics in children with an OCD is particularly frequent (20 % to 30 %). The association with chronic motor tic disorder or Tourette syndrome is rarer (4 % to 5 %), but is, however, overrepresented in relation to the general population. This association could represent a particular form of OCD as much in clinical terms (early onset, male predominance) as in pathophysiological terms (common genetic vulnerability).

A history of ß-haemolytic streptococcal infections is frequently found in children affected by OCD. It has been suggested that OCD may be caused by an autoimmune response in a sub-group of patients. These patients may be characterised by a special vulnerability in the immune system, marked by D8/17 lymphocyte overexpression. This mechanism would be common to different clinical pictures classified by the term PANDAS (*Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections*).

The initial diagnostic difficulty, the significance of the effects of the disorder and the plurality of the mechanisms involved justify a careful evaluation of children affected by OCD. Diagnosis remains a clinical procedure, but tools do exist at present, of the assessment scale type, that have been thoroughly validated for these children. The most up-to-date is the YBOCS scale (*Yale-Brown obsessive-compulsive scale for children*), which assesses both aspects of the disorder. There is also a version for children of the Leyton obsessive inventory self-questionnaire. A systematic search for associated psychiatric and neurologic disorders is broadly recommended.

Overall, studies performed in recent years underline the relative frequency and the short and long-term effects of this disorder in children. If importance is to be ascribed to age-related features of the condition, the relevant studies now underline the developmental consistency of this disorder, even if early-onset forms may involve a separate aetiopathogenesis.

What would assist in the early detection of anxiety disorders?

Emotional disorders in children are generally difficult to perceive by those around them (parents, teachers), who tend to minimise the severity of the disorders. Many studies show that the most children presenting with anxiety disorders are not recognised as such, and that they either receive no treatment or inappropriate treatment. A delay of several years is generally reported between the onset of the disorders and the start of appropriate management. Sometimes it is only when complications occur (disorders of social adaptation, refusal to attend school, behavioural disorders, depressive disorders, eating disorders) that anxiety disorders are identified. Because somatic complaints are frequently associated with anxiety disorders and because diagnosis of the latter is poorly understood, these children may also be subjected to useless investigations and to improper treatments, which cause their own particular adverse effects.

Anxiety is not only a normal phenomenon, but also serves a purpose and is adaptive. During childhood and adolescence normal forms of anxiety, corresponding to the different stages of development achieved, will be observed. Anxiety disorders such as separation anxiety, social phobia or specific phobias contrast with a developmental anxiety of an equivalent intensity, but distinguishing these anxiety disorders from normal developmental fears is not always easy.

Separation anxiety disorder is the anxiety disorder most frequently found in children and adolescents. The mean age of onset of the disorder is around 6-7 years, although onset in adolescence is not unusual. If it does occur spontaneously, separation anxiety most often occurs following a stressful life event involving a change in the child's attachment profile. The essential characteristics of separation anxiety consist of a clinical picture in which the main disturbance is an excessive anxiety when the child is separated from the people to whom he is principally attached. Its diagnosis is based on three orders of signs: manifestations of intense distress on separations or when a separation is feared; morbid thoughts and preoccupations about the integrity of the family in particular and the integrity of the child himself and a nostalgia for home and an intense desire for the family to be together. It is implicitly accepted today that there is a continuity between developmental separation anxiety (the normal distress reaction observed in babies separated from the physical presence of their principal attachment figure) and separation anxiety disorder. Two types of criteria are used to distinguish them chronologically: separation anxiety disorder occurs either as an extended and abnormal persistence of a separation anxiety which began during the appropriate developmental period, or as the resurgence of separation anxiety reactions at an age when these are normally moderate or absent. Furthermore, separation anxiety disorder is distinguished from developmental anxiety disorder by the intensity of its manifestations and its effects on the child's functioning. Separation anxiety disorder is observed more frequently in girls than in boys. If it does disappear spontaneously, its course typically extends over several years with an alternation of periods of remission and exacerbation promoted by trigger factors. An increasing number of studies appear to indicate the presence of a predisposing factor, which is particularly important to the later development of anxiophobic and depressive disorders.

The mean age of onset of social phobia is between 12 and 15 years, but two peaks in frequency are noted, one around 5 years and the other around 13 years. The essential clinical feature of social phobia is a persistent and intense fear of situations in which the child is in contact with unfamiliar people or may be exposed to attention and observation by others (the anxiety must occur in the presence of other children and not only in relations with adults). In children social phobia is generally diffuse and involves fear of not knowing how to defend themselves, of being the "scapegoat", of being rejected, of not having friends. The situations feared in the school context are particularly frequent (fear of speaking up, of going to the blackboard, of reading aloud, of asking for information, of playing sports, of taking

part in an outing or a group activity). In adolescents it can take on a more specific character. It involves physical appearance in particular, contacts with the opposite sex, the act of speaking with people in authority and social and/or intellectual performance. Distinguishing social phobia from developmental social fears and from shyness (which is a non-pathologic behaviour particularly frequent in children and adolescents) is not always easy. The children in question are very unobtrusive and reserved in class and so are rarely reported by teachers. Certain signs should attract attention: persistent fear of the unknown or of the unfamiliar, although relations with familiar people are of high quality; a persistent fear of judgement on the part of those close to them and persistent withdrawal in relation to unfamiliar adults and children of the same age. Essentially, it is the intensity of the feeling of suffering in particular and the significance of the effects of the manifestations of social anxiety on the child's habits, his relationships with others and his social and/or school activities, which favour a diagnosis of social phobia. The course of social phobia is always chronic.

Most specific phobias (fear of the dark, animals, of possible injury, of blood, of the dentist, of examinations) are encountered during childhood. The mean age of the onset of the disorder is generally between 6 and 12 years. The essential clinical feature of specific phobias is an intense and persistent fear, irrational in nature, triggered by the presence of, or anticipation of confrontation with, a specific object or situation. Confrontation or anticipation of confrontation with the phobogenic stimulus provokes in the child a fear or excessive fright, translated physiologically by intense neurovegetative phenomena. As a general rule, the more severe the phobia, the more extensive the avoidance behaviours are and these can interfere with the child's functioning. In terms of quality there does not appear to be any difference in nature between specific phobias and developmental fears. This means that diagnosis of specific phobia is based above all on quantitative criteria: persistence of the disorder (at least six months) and severity of the disorder (intensity of the child's feeling of distress, significance of the effects of the disorder on his habits). In children, specific phobias are unstable. They may occur without apparent reason and disappear just as mysteriously. Certain phobias, such as phobia of blood and physical injuries may, however, persist to adulthood. The attitude of those around plays an important role in the course of the disorder.

Panic attacks are defined as paroxysmal anxiety crises, that occur suddenly and whose course is brief, combining somatic and cognitive manifestations (the latter may, however, be absent in the young child). Isolated panic attacks are frequently observed, in adolescents in particular. Panic disorder is characterised by recurrent and unexpected panic attacks, accompanied by one of the following symptoms: persistent fear of having other panic attacks, preoccupation with the possible implications of the panic attacks or their consequences and a significant change of behaviour in relation to panic attacks. By reason of their cardiac, respiratory, gastrointestinal and neurological manifestations panic attacks in children and adolescents present difficulties of differential diagnosis against diverse organic conditions and are often ignored. Ignorance of this disorder at this time of life frequently leads to diagnostic errors, to a multiplication of invasive examinations and improper treatments, and to a delay in the administration of an appropriate therapy. While authentic panic disorders have been reported in prepubertal children, the mean age of onset of the disorder is generally between 15 and 19 years. Retrospective studies support a chronic course for the disorder, dominated by recurrent depression and the development of agoraphobia with extensive avoidance. Panic disorder is observed more frequently in girls than boys.

Hyperanxiety disorder in children is considered the equivalent of generalised anxiety disorder in adults. Its mean age of onset is around 8-9 years. Hyperanxiety disorder is characterised by excessive anxiety and worries about a certain number of events or activities

(like work or school achievements), occurring most of the time over at least 6 months, these preoccupations being difficult to control for the subject. In addition, at least one of the following symptoms must be present: agitation or sensation of being over-excited or at the end of one's resources, fatigability, concentration difficulties or gaps in memory, irritability, muscular tension, sleep disturbances. Approximately 50 % of hyperanxious children continue to present with difficulties at the time of adolescence. Certain authors view this as a prodromic stage foretelling other disturbances.

For a long time the presence of post-traumatic stress condition in children was unacknowledged, parents, teachers and even health care professionals tending to minimise the traumatic impact of the stressful events with which the child may be confronted. Typically the events capable of engendering a state of post-traumatic stress in children and adolescents include being the victim of, or witness to, an act of violence. But a child may also develop a post-traumatic stress condition by indirect confrontation with a stressful experience, an event which he just escaped, the death of, or an accident involving, someone close to him, which he did not take part in. The development of a disorder is then promoted by its repeated and detailed evocation by those around him and the media. For some authors the child's reactions to a stressful event depend not so much on his degree of exposure to the risk than on his actual experience and his feelings at the time of the event or on the occasion it is evoked. The signs and symptoms of post-traumatic stress condition are always grouped around three main dimensions: reliving the event, avoidance behaviours and numbing of general reactivity and neurovegetative hyperactivity. In children, however, the clinical picture is frequently not complete. All the authors agree in saying that whatever the signs and symptoms presented, these children should be treated, so great are the consequences of this disorder for the child's functioning and later development. It is normal to describe in children two main clinical forms of the post-traumatic condition, according to the nature of the trauma experienced. The child may be exposed to a single traumatising event (type 1 trauma: natural catastrophes, abduction, accident) or be subjected to repeated trauma (type 2 trauma: physical abuse, sexual abuse, war, internment). In type 2 trauma the setting up of defence/adaptive mechanisms (denial, repression of effects, identification with the aggressor, aggression against oneself) will lead to progressive personality modifications. The onset of the disorder usually occurs immediately or a short time after the traumatic event. It may, however, sometimes occur after a latency period of some months, if not some years, during which less specific signs and symptoms are frequent (sleep disturbances, irritability, social withdrawal). Separation anxiety or hyperanxiety appearing following a traumatic event must give grounds for concern about the development of deferred post-traumatic symptoms. If the intensity of the post-traumatic symptoms most often appear to grow weaker with time, in approximately 50 % of cases the disorder will persist for more than 12 months after the trauma. Initial, severe post-traumatic signs and symptoms appears to be strongly predictive of a prolonged course. In the same way, certain stimuli recalling the event and the occurrence of new stressful events may help to reactivate the signs and symptoms and to perpetuate the disorder.

Despite instruments specifically intended for children and adolescents having been developed in order to facilitate the detection and clinical screening of anxiety disorders, their use still raises numerous problems. Self-questionnaires, constructed to enable a quantification of anxiety, can in no case be employed for a diagnostic purpose. They provide a measure of the general intensity of the child's anxiety, they do not allow us to discriminate between children with an anxiety disorder and children with other psychiatric diagnoses. Only standardised diagnostic interviews allow precise evaluation of the anxiety disorders. Their reliability does not appear, however, to be particularly high before the age of 12 years and their use should be reserved for qualified and trained practitioners.

What would assist the early detection of affective disorders?

The psychosocial effects and, at times, chronic or recurrent course of affective disorders in children and adolescents makes their early recognition and appropriate treatment imperative. The prevalence of depressive disorders increases in adolescence, and a female preponderance emerges at the same time. Bipolar disorder begins in adolescence in 30 % of cases. Clinical expression of the depressive signs and symptoms may vary during development; the younger the subject the more likely it is to be "behavioural". The clinical features are similar to those seen in adults in the severe forms and in adolescence. The "core symptoms" of depression (depressive mood, suicidalideation, psychomotor retardation) are the least influenced by age. International classifications use the same criteria, with some minor adaptations, whatever the subject's age, but may, by virtue of this, under-diagnose depressive disorders in young subjects. Apart from the depressive signs and symptoms themselves, with their developmental variations, psychiatric comorbidity or a suicide attempt are important warning signs for an early diagnosis.

In children and adolescents, comorbidity rates are high. Anxiety disorders and disruptive behavioural disorders (oppositional behaviours, behavioural disorders andattention deficit hyperactivity disorder -ADHD) are the diagnostic categories most frequently associated with affective disorders. Generally they precede the affective disorder, in contrast with substance abuse, which may occur during its course. The connections between ADHD and bipolar disorder have yet to be defined. Comorbid disorders often have a more vigorous clinical expression than depressive symptoms and may be the primary reason for care seeking.. This is also the case for suicide attempts, which involve about 40 % of depressed children and adolescents.

Beyond early diagnosis of a recognised depressive disorder, identification of children and adolescents "at risk" for an affective disorder could be of value in terms of prevention. The occurence of a major depressive disorder is attributed to a conjunction of individual and/or familial vulnerability and precipitating factors such as life events. Numerous familial, temperamental and cognitive variables play a role in depressive vulnerability. However, their predictive value and their specificity with regard to the occurrence of an affective disorder vary. For example, there are many arguments implicating a pronounced emotionality (and to a lesser degree low sociability and inhibition) in the occurrence of disorders on the anxiodepressive spectrum. The low predictive value of this temperament trait makes it inapplicable, however, to a preventative approach. It is necessary, therefore, to pay further attention to the conditions that precipitate the expression of vulnerability in terms of psychopathology. Some of these are valuable for the early diagnosis and prevention of affective disorders in children and adolescents.

Vulnerability factors in affective disorders, which can be employed in its prevention

- Subclinical depressive signs and symptoms, which may be accessible to a dimensional assessment
- A family history of depression or of another mental disorder, especially in first-degree relations. The impact of a depressive disorder in a parent may be direct, as mediated by genetic factors, or indirect, via deterioration in parental care for example.
- Unfavourable psychosocial conditions, chronic stress
- Other mental disorders likely to be complicated by depression

The most widely used procedure at present in the screening of depressive disorders in large samples comprises two stages: screening by self-questionnaire followed by a structured or semi-structured diagnostic interview.

How can we predict the course of an eating disorder towards a pathologic form?

Eating behaviour depends on individual genetic and psychological factors, in close interaction with familial and sociocultural environmental factors. Eating disorders (ED) form part of a polyfactorial aetiopathologic model, which must be integrated in all its diversity in order to address screening and prevention.

Epidemiological data suggest that eating disorders be considered as a continuum from the normal to the pathologic, within a dimensional system rather than one that is merely categorical. Indeed, the categorical approach essentially classifies known forms, but does not include the anorexic or bulimic behaviours that are extremely frequent or changes in eating habits in the context of reactional or situational depression. These behaviours are not without risk of self-reinforcement and may change into organised pathologic forms. Approximately 5 % of young women present symptoms of anorexia nervosa without meeting all the diagnostic criteria and frenetic eating behaviours are very frequent (40 % of a schoolgirl population in the United States for example). With regard to France, in a previous survey involving 35,000 school children in Haute-Marne, the authors found that one out of three young girls was preoccupied with her body, 20 % experienced restrictive behaviour and fasting without meeting the criteria for specific pathology, 3 % experienced vomiting and abuse of laxatives or diuretics and almost 10 % had a weekly bulimic crisis.

The comorbidity of eating disorders and depression has been demonstrated. The prevalence of depression in the disorders is far in excess of that found in the general population. According to studies, 11 % to 66 % of young women who have been diagnosed as suffering from an eating disorder, suffer a major depressive episode, the frequency being higher in bulimic patients. In four out of seven longitudinal studies, a drop in self-esteem precedes the occurrence of an eating disorder. However, the frequently associated depression, - which is often confused with a drop in self-esteem - is not itself predictive of eating disorders. The authors, as a whole, emphasise that frequency of an addictive comorbidity in patients suffering from bulimia is by no means negligible. Addiction involves drugs, alcohol and, to a lesser degree, psychotropic medicines such as amphetamines, tranquillisers and even barbiturates. Psychoactive substance abuse is estimated to involve between 30 % and 37 % of bulimic patients, and between 12 % and 18 % of anorexic patients (by way of comparison, less than 20 % of adolescents who consume psychoactive substances develop abuse or dependence).

The period of adolescence in girls is a risk factor for eating disorders. Future anorexics and bulimics experience puberty – the key time of their physical and psychic maturation – as more difficult, than other girls do. Their difficulties seem to be focused on body image and self-image, which are intimately connected at this age.

The role of sociocultural factors is difficult to detect, even if several studies have shown that eating disorders were more frequent in certain environments where professional activity centres around the body (dancers, models, high level sportsmen and women). An increase in the frequency of eating disorders, addictions and suicidal behaviour appears to occur in parallel to the adoption of western modes of living. This underlines the addictive and social dimension of eating disorders.

The frequency of a family history of mental disorders in patients presenting an eating disorder is acknowledged. The disorders involved are depression (25 % *versus* 8 %), alcohol addiction and drug abuse. Frequency is higher in bulimics than in anorexics. The family dynamic is very strongly implicated, but it is not known whether this is as a primary ("the family is partly at the root of the eating disorder") or secondary factor ("the girl's eating

disorder disturbs the family"). The families of bulimics are more disorganised and their characteristics are those of their children. The families of anorexics have more problems with anxiety and control; references to the ideal play a much more restrictive role, although these elements are not highly specific. The role of sexual abuse during childhood in the pathogenesis of eating disorders has been noted. Approximately 30 % of patients present with such a history. However, comparison of bulimic patients with subjects suffering from other mental disorders has shown few differences, which indicates that the relationship between sexual abuse during childhood and eating disorders is not specific in terms of co-occurrence.

Genetic vulnerability factors are essentially expressed in disorders with an obsessive and depressive dimension corresponding to pure restrictive anorexia nervosa. "Perfectionism" is a frequent personality trait in anorexia. The borderline type personalities, in which environmental influence is prevalent, are more readily found in the *purging type* of anorexia nervosa and in bulimics. A recent study, performed on a sample of 210 subjects, reported a 27% prevalence of personality disorders in eating disorders. Anorexic-bulimics more frequently suffer from a personality disorder (39 %) than bulimics (21 %) and anorexics (22 %). Anorexics (for whom no borderline personality is found) most often belong to cluster C (avoidant, dependent, obsessive-compulsive and passive-aggressive personalities), while bulimic subjects are mainly found in cluster B (borderline, histrionic, narcissistic and antisocial personalities). In fact, many clinical features are common to bulimia and the *borderline* personality: affective instability, impulsivity, consumption of substances and pathologic behaviours such as theft or suicide attempts.

A study published by an English team investigated vulnerability factors that could be specific. A very low self-esteem and a high level of perfectionism differentiated anorexic subjects from subjects suffering from other mental disorders. The following are found in bulimic subjects: a greater vulnerability to familial or social influences that set value on diets and slimness (which is not found for anorexia nervosa); a higher frequency of negative remarks from those around the child on their physical appearance as well as more obesity in their parents and during childhood and a slightly earlier age at menarche. These vulnerability factors seem to form an "at risk mental state" but the point of transition towards acknowledged disease remains unspecified.

How is it possible to identify, during childhood, the predictive signs of a risk of schizophrenia?

Schizophrenia is a disease that generally begins at the end of adolescence or the beginning of adulthood. Although the validity of the diagnosis of schizophrenia in children appears to be clearly established now, its occurrence at this time of life is still relatively rare. It is estimated that the prevalence of early onset schizophrenias, during childhood, is 50 times lower than that of adult onset schizophrenias.

The emergence of developmental psychopathology and data from studies of children at risk of schizophrenia have led to a clear formulation of the problem of the differential expression of this disorder according to age and developmental stage. In the same way, clinical similarities observed between the early onset and normal forms of schizophrenia have also led to proposals for aetiopathogenic hypotheses from the developmental point of view.

According to the neurodevelopmental model currently proposed, anomalies affecting cerebral development in the course of the first years of life remain relatively dormant in clinical terms for a long period. The appearance of the characteristic symptoms of the

disorder is then connected with the cerebral modifications of normal maturation in adolescence or at the beginning of adulthood. These hypotheses have led to much research aiming to identify the early predictive signs of a later course towards schizophrenia.

Many retrospective studies have tried to retrace the premorbid history of adult subjects who have developed schizophrenia. Their results appear to be extremely disparate, the symptoms found in the childhood of schizophrenic subjects being multiple, non-specific and variable according to age and gender. They include: psychomotor developmental delays and disorders; language delays and disorders; flat, expressionless gaze; early feeding difficulties; sleep disorders; enuresis; concentration disorders; formal thought disorders; almost "delirious" ideas; difficulties in adaptation and poor educational achievements; disorders of socialisation; behavioural disorders and anxiety disorders. More recent cohort studies confirm that the childhood of future schizophrenic subjects is clearly differentiated from that of the general population on many points: delays and disorders of psychomotor development, cognitive deficits and behavioural disorders. On this account therefore, relational difficulties and those of social adjustment (preference for solitary games being observed even before the age of 14 years, particularly marked disturbances in relations with peers and unfamiliar adults, poor social functioning at the age of 16-18 years) appear to be one of the most frequent precursors found in children and adolescents who will develop schizophrenia in adulthood. Independently of these relational difficulties, an abnormal distrust and sensitivity also appear to be particularly important risk factors for the later development of schizophrenia (the latter data should be compared with past experiences reported by adult schizophrenic patients who describe themselves as particularly mistrustful and sensitive during childhood).

Studies have been performed on the course of children who have a schizophrenic parent and are thus at high risk of presenting with the disorder. These studies show that children who actually develop schizophrenia in adulthood present with delays in different areas of development and a less effective social adaptation compared to controls. Several studies have individualised a dysmaturation syndrome called "pandysmaturation", which is found in almost half the children of schizophrenic parents and, more particularly, in those who will develop a schizophrenia in adulthood. This syndrome brings together transitory delays followed by an acceleration and a return to normal levels in motor and/or visuomotor development, an abnormal functional profile at general developmental examinations (with failures in simple psychological tests and successes in more complex tasks) and retarded skeletal growth. Similarly adolescents at high risk of schizophrenia present significantly more frequently with minor physical anomalies (increase in cranial perimeter, hypertelorism) and minor neurological signs (in particular in the sphere of sensory integration). Other signs with a significant predictive value have also been found in these children: neuropsychological deficits affecting verbal memory, attention and global motricity; behavioural disorders and difficulties with social adaptation. The children are described as solitary, passive, rejected by others and as having discipline problems.

More recently, several studies have been concerned with the nature of the prodromic symptoms that occur during the year preceding the first psychotic episode. The most frequent symptom appears to be social withdrawal. However, numerous other symptoms can also be observed: sleep disorders, anxiety, irritability, depressive mood, blunted or inappropriate affects, reduction in attention and powers of concentration, obsessive-compulsive symptoms, suicidal notions, bizarre ideas and behaviour and carelessness.

Taken separately the predictive and warning signs of the normal forms of schizophrenia identified in all these studies appear in reality to be relatively non-specific and can be observed in children and adolescents who will develop other mental disorders. It is also true

that the study of children affected by schizophrenia confirms the hypothesis that signs and symptoms could vary according to the stage of development. So, do children affected by schizophrenia more frequently present in early childhood with language delays and abnormalities, a psychomotor delay with hypotonia and a lack of sensitivity and bizarre responses to environmental stimulations. During later childhood a lability of mood, inappropriate grasping reflexes, unexplained angry reactions and hyperactivity appear. Later, loss of train of thought, constricted or inappropriate affect, followed by hallucinations and the delirious ideas characteristic of the disorder occur.

All these data have led in recent years to the development of early intervention programmes. The latter, however, in our present state of knowledge, raise numerous ethical problems: risk of iatrogenic effects (social stigmatisation, adverse effects of neuroleptics), "false positives" and lack of data on their efficacy and cost.

Comprehensive educational programmes may reduce the cognitive, communicative, social and behavioural handicaps of autism.

The aim of the educational approaches in autism and other pervasive developmental disorders is to allow the child to realise his maximum potential and to promote his independence and integration in society, while reducing the incidence of secondary handicaps.

The upbringing and education of these children requires special skills, which are not part of the ordinary repertoire of parental capabilities, and which often go beyond the techniques regularly taught in traditional professional training courses. The efficacy of the interventions depends on the availability and the adequate training of competent professionals organised within accessible departments.

The principles of educational treatments aim to improve the child's communication abilities, by developing his language, and by using different systems to increase his ability to communicate (signs, *Picture exchange communication system*, visual symbols, gestures). The promotion of social interactions is another fundamental component of the educational programme, by developing social competence in very intense and highly structured interactions between parents and children. Secondarily, this competence is progressively transferred into other one-to-one relationships, in more ecological and natural environments, and finally into relationships with peers of the same age in wider groups. The reduction in routine and obsessive activities is a third part of the intervention, a way of limiting the time the child spends in repetitive activities marked by social isolation, a lack of reference to others and of the observation of the material and human environment which, at this age, is an important source of information necessary to development.

The educational programme should be adjusted to the individual, with short-term support for emerging abilities, and periodic re-evaluation of new acquisitions and needs. Close collaboration with the family environment is a characteristic of all educational interventions, which aim in particular to facilitate the general application of capabilities in a wide range of contexts, which is often difficult for these children. Furthermore, an effective collaboration between professionals and families permits a reduction in the latters' stress levels and allows them to lead a family life that is as harmonious as possible where each member of the family (in particular brothers and sisters) can blossom normally.

Early intervention programmes appear, on the whole, to be associated with substantial progress in the cognitive and language development of children suffering from PDD, and progress is generally maintained after the end of treatment. An early age at the start of

treatment seems to be a necessary condition for effective intervention. Programmes ensuring treatment at the level of 20 to 25 hours a week yield positive results. Considerable progress is also made, however, through markedly different programmes (both in philosophy and method); it is possible that these programmes have certain principles and educational methods in common, which it is absolutely imperative to identify now. While treatment needs to commence early, it is difficult to state definitively at present that treatment should begin at 2 years rather than 3. As equally significant results are obtained in the programmes administered at home or in professional centres, it is equally difficult to make a formal prescription regarding the best place for these interventions to begin. The family's choice should be respected in this matter. In addition, whatever the place selected, close co-operation is necessary between professionals and parents over a long period of time. Even if a programme begins at home, its aim is generally to prepare the child for life and education in the school environment, to facilitate his transition from home to school, to reduce progressively his level of support and to promote the employment of his abilities in increasingly natural and varied environments and situations. Several authors note that progress is often more impressive in children who have a generally lower level of functioning at the beginning. In other words, there are factors connected with the child's biological and psychological equipment which interact with his response to treatment.

The initial results of an evaluation of educational programmes indicate, therefore, that very early interventions (before 4 years and if possible earlier still) lead to considerable progress. The methodology of each of these evaluative studies has certain limits, but the convergence of the results of one study with another appears to indicate that substantial gains, notably on the cognitive and communicative levels, may be obtained through educational interventions that are sufficiently early and intense. A certain number of questions remain which research studies are investigating. Priorities for further study include the optimum intensity of the intervention, the age at which it should be established to maximise its effects, the ideal place for the intervention (at home or in class), the nature of those aspects of the educational programme which are absolutely necessary for its efficacy, the applicability of these programmes to all children affected by PDD and their long-term effects.

Prevention programmes are being developed adapted to the child's level of risk in relation to anxiety or affective disorders.

Empirical research bearing on the aetiology of anxiety disorders in children has enabled a certain number of risk factors to be identified (a family history of affective disorders, a child frequently confronted with stressful life events). Different prevention programmes have been developed, most often founded on cognitive and behavioural techniques, whose aim is to reduce the impact of these risk factors while optimising the child's competences in terms of adjustment and adaptive strategies. The interventions may focus on the child himself, his parents and/or his environment. Several types of programmes have been developed according to the target populations. Some are intended for the total population of children and adolescents (what is known as "universal" prevention). Others focus on children and adolescents assumed to present with risk factors (what is known as "selective" prevention). A third kind deal with children and adolescents who are at high risk of presenting with clinical and/or laboratory markers of vulnerability or who already manifest anxiety symptoms (what is known as "indicated" prevention). If an evaluation of these programmes yields results that are encouraging, supplementary studies are indispensable to specify the long-term efficacy of this kind of action.

Prevention programmes for affective disorders are beginning to be developed on the basis of

cognitive and behavioural interventions that were initially developed for depressed young people. An initial type of programme is intended for families where at least one parent suffers from a depressive disorder. It is focused on parentality and parent-child interactions. A second type of intervention is proposed for children and adolescents in whom subclinical depressive signs and symptoms have been identified by self-evaluation questionnaires. These programmes combine learning cognitive techniques for problem solving, strategies for social communication and the fight against depressogenic cognitive schemas. Evaluation of these programmes, which are still small in number, yields encouraging results at least in the short term, especially for participants who initially had the highest scores for depression.

Recommendations

To ensure that every child has the best chance of starting life in good health is a major aim of public health. Mental health, an integral part of general health, is essential for a child's development and educational success.

At the beginning of the XXth century pre-school medical examinations were introduced in Europe. Initially focused on the reduction of malnutrition, physical diseases and handicaps that could compromise a child's education, these health assessments were then extended to include an examination of the child's psychomotor development.

In France, the detection of mental disorders in the general population should be able to rely on existing systems for the systematic monitoring of children from birth to adolescence. This system should benefit from advances in knowledge of child development and the development of validated indicators. It should also take into account the risk factors that may be associated with mental disorders.

Today it appears necessary to involve all education and health care professionals in the promotion of mental health in children and to educate them to recognise the early signs of emotional and behavioural problems. By publishing this summary the expert group advocates informing and educating all those involved in contact with children : parents, teachers and special needs staff, who are in the best position to identify the first signs of a mental disorder; GPs, paediatricians, school and PMI doctors, capable of recognising this kind of disorder and to refer the child to the appropriate structures for diagnosis and management; and finally paedopsychiatrists, who are in a position to translate research results into their clinical practice.

Management in a specialist environment of children and adolescents presenting the warning signs of mental disorders should provide every guarantee of expertise for a rapid diagnosis that makes early intervention possible. It should also be accompanied by follow-up to prevent the appearance of other disorders, since comorbidities are very frequent. Finally, children with a parent, brother or sister in follow-up for a mental disorder should be paid special attention.

The group of experts emphasises the need for a better knowledge of the French situation in terms of the prevalence, incidence and course of mental disorders and, in order to achieve this, for validation of the tools for detecting disorders in the French context. It scrutinizes the value of longitudinal studies to identify the impact of various factors (genetic and environmental) and their interactions in the development of mental disorders. It also notes the pertinence of clinical research to the predictive value of certain early signs. Research into the mechanisms underlying mental disorders should integrate the various disciplines investigating brain function (neurobiology, imaging, neurocognition, experimental psychology) and also use new animal models of developmental anomalies.

Training and information

HEIGHTEN THE AWARENESS OF PARENTS, TEACHERS AND SPECIAL NEEDS STAFF SO THEY CAN IDENTIFY DEVELOPMENTAL DISORDERS IN CHILDREN

Some young parents are powerless as far as recognising a mental disorder in their first child

is concerned. Television broadcasts, like magazines, contribute, thanks to effective popularization of these issues, to making parents aware of disorders that were previously poorly understood. Mental health is not perceived in the same way as it was, attitudes in general have changed and the younger generations find it easier to accept that their problem is a psychological one. The expert group advises setting up an institutional site on the Internet for the information of future parents.

In order to initiate dialogue with the doctor or paediatrician the parents could be induced to share their observations on their child's behaviour by means of filling in a commented questionnaire with the doctor at every visit. The expert group recommends deciding which items (ten at the most, given the time the doctor has available) should appear on this questionnaire intended for parents.

The evaluation booklets already available in certain nursery schools could form a valuable tool for bringing to the fore dysfunctions in the sensorimotor, cognitive and affective development of children. The expert group recommends that the items listed in the nursery school evaluation booklets be analysed and (re) drafted in such a way that they allow an objective evaluation of the child's developmental status.

IMPROVING THE ABILITY OF DOCTORS (GENERAL PRACTITIONERS, PAEDIATRICIANS, SCHOOL AND PMI DOCTORS) TO REFER CHILDREN LIKELY TO BE SUFFERING FROM A MENTAL DISORDER TO THE RIGHT PERSON

The initial examination of the infant (within the first eight days of life) is performed by a paediatrician in 90 % of cases. The examinations performed in the first two years of the child's life are performed in 60 % of cases by a general practitioner. Then the PMI doctors and school doctors take over. The initial education of doctors currently includes an insufficient number of teaching hours for learning about mental disorders, given the prevalence of these disorders in the general population. Psychologists should also have sufficient training to allow them to recognize mental disorders. The expert group recommends aiming to ensure that the training given in the course of the study of medicine and psychology is appropriate to the kind of work that awaits the various professional groups in their practice with children. It recommends consolidating and standardising in all French faculties training in the cognitive and socio-affective development of children. Adapting training in this way should make it possible for practitioners to detect a mental disorder in a child in order to refer him to a specialist.

The general practitioner or paediatrician should have the necessary time available to evaluate, among other things, the quality of interactions of the baby or child with those around him. The expert group recommends that time spent in identifying risk factors and signs of a mental disorder should be recognised as a medical act entirely in its own right, and recorded as such in the nomenclature.

PROMOTING THE CONTINUING EDUCATION OF PAEDOPSYCHIATRISTS IN NEW KNOWLEDGE ABOUT MENTAL DISORDERS IN CHILDREN

Diseases such as autism, hyperactivity, anxiety disorders, affective disorders, eating disorders, obsessive-compulsive disorders and schizophrenia are among those that necessitate assumption of the heaviest financial responsibilities in public health terms. Late diagnosis often has detrimental effects on prognosis. It seems necessary then to give paedopsychiatrists the means of early recognition of these disorders in children.

Advances in scientific knowledge in the fields of the identification of environmental and genetic risk factors and of the biological bases for cerebral development, the contributions of the cognitive sciences and of functional imaging improve our understanding of mental dysfunction. Research results should be able to be rapidly translated into clinical practice.

In order to improve diagnosis of mental disorders in children, the expert group recommends that specialists benefit from new scientific and medical advances, by diffusion and training in recently acquired knowledge. For example, data obtained from cerebral imaging of mental disorders in children and adolescents, and more generally that concerned with cerebral maturation, are not part of conventional teaching of the specialist studies in psychiatry and paedopsychiatry. The participation of researchers in educative activities would permit the knowledge conveyed to students in a speciality to be translated into effect.

General population screening

ADDITIONS TO THE FRENCH SYSTEM OF SYSTEMATIC SURVEILLANCE OF THE MENTAL HEALTH OF CHILDREN

Regulations, differing according to the country, are in existence on the subject of monitoring children. In France, compulsory systematic examinations are performed at birth, at months 9 and 24, at 5 – 6 years (before entry to primary school) then at 11–12 years old. Other examinations are recommended or proposed without being compulsory (examination at 4 months, examination at 18–24 months in the Ile-de-France only, examination at 3–4 years)

It could be worth making available a tool that permitted a developmental "score" to be established for the examinations performed in the course of the first two years. A break in the progression of this score, and not the child's position in relation to a "mean", could sound the actual alarm signal. The expert group recommends that the indicators of the child's sensorimotor, cognitive and emotional development be integrated into items in the examinations performed in the first two years of life. These indicators should be determined beforehand by an *ad hoc* working group.

An examination of the surveillance programme for the first two years reveals an absence of systematic follow-up between 9 months and 24 months. Now a certain number of diseases emerge at this age, in particular autism and language disorders. The expert group recommends studying the possibility of integrating a medical examination of the child into the course of his second year (at around 18 months). In addition, the examination at 24 months is probably too early to detect any possible language disorders. An examination at about 30 months of age would allow the latter to be detected.

With regard to the examinations performed on starting school (nursery school), it would be advisable to make teachers aware of the value of exploring the richness of the child's vocabulary by the creation of some items that permit recognition of potential dysfunction. The expert group draws attention to the value of this kind of identification since potential disorders are likely to affect the beginning of school education. In addition, hyperactivity can probably be identified from the age of 3 or 4 years onwards.

The examination before entry to primary school is important. It gives the school doctor an opportunity to focus on attention and behavioural disorders. Language disorders, unnoticed at the first nursery school examination, may still be detected. The expert group recommends that the content of the compulsory medical examination on entry to primary school be standardised between the different educational establishments, and be performed in the

presence of teachers and parents. It also advises that a booklet be drawn up as a tool for nurses, school doctors, teachers and parents, which would contribute to keeping them informed on the disorders that can be expressed at this age.

During adolescence, several disorders may appear, like eating disorders, panic disorder or the consumption of psychoactive substances which justify a systematic examination of adolescents. The expert group draws attention to the value of an overall assessment of adolescence, before the end of compulsory schooling, in all educational establishments in France. Detection should be accompanied by educational and health measures

THE DEVELOPMENT OF TOOLS WHICH MAKE IT POSSIBLE TO IDENTIFY MENTAL DISORDERS IN THE CONTEXT OF THE SYSTEMATIC MONITORING OF CHILDREN

In the 9th month, attention, memory and learning abilities can be explored thanks to various standardised tools that can be applied today at a very young age by trained psychologists. A deficit in some of these abilities may predict serious difficulties later, and necessitate special follow-up. The expert group recommends that indicators allowing an evaluation of attention and memory be made part of the examination at 9 months.

At the systematic examination at 24 months some new items can be included which would allow autistic disorders to be identified. Data does in fact exist showing the value of certain tools for the detection of autism that can be applied from the age of 18 months. The expert group recommends that new items be established in the systematic examination at 24 months for the detection of autism on the basis of current instruments validated in the French context.

It is possible to detect hyperactive children at the examinations at 4 years (nursery school) and at 6 years (before starting primary school), since manifestations of hyperactivity can be discovered from the age of 3 years onwards. It should be made clear that children in whom hyperactivity is identified at the age of 3 or 4 will not systematically progress to an obvious disorder with effects on their education, which would not, then, be diagnosed later. The indicators used must permit identification of manifestations of the motor type (falls, domestic and road accidents, inability to remain still, difficulties in concentrating on tasks needing less than 10 minutes' attention…) and of difficulties in the acquisition of language (delayed speech). The expert group recommends the development of a learning package for evaluating development, which is simple for the GP or paediatrician to use (the shape-fitting game type) which would allow identification of hyperactive children in particular in the course of the examinations at 4 years and 6 years.

At the age of 11-12 years, identification of attention disorders and anxiety disorders in the pre-adolescent can be based on a significant falling off in school results in the 6th or 5th: the child no longer learns. The expert group recommends considering a falling off in school results as a warning sign of attention disorders and anxiety disorders at the age of 11-12 years.

For the assessment at adolescence, it would be possible to detect eating disorders from the age of 12.5-13 years using five questions established on the basis of a tool like SCOFF (*Sick, control, one stone*[1]*, fat, food).* Validation of this questionnaire in the general population and in France is underway. It can deal only with the identification of recognised forms of anorexia and bulimia. Detection of affective disorders (from 15-16 years onwards) and that of anxiety disorders could be achieved on the basis of a few predictive items defined using tools

[1] English unit of weight equivalent to 6.348 kg

evaluated on the general population. The expert group recommends adapting to the French context the tools for detection that have already been validated for 12-17 year olds in the general population, which make it possible to identify affective disorders, anxiety disorders and eating disorders.

Identification of mental disorders in the context of systematic assessments in the general population must of necessity be continued by follow-up by a specialist, the only one in a position to make a diagnosis.

TAKING INTO CONSIDERATION CERTAIN RISK FACTORS IN THE CONTEXT OF MONITORING THE GENERAL POPULATION

Repeated stress, in the family environment or outside the family, bereavement, divorce, abuse, moving house, hospitalisations, disasters, stress of school environment, certain serious and chronic diseases, lack of affection, cultural maladjustment may be risk factors for the development of certain disorders. The expert group recommends that risk factors from the family environment be brought to the attention of medical personnel responsible for monitoring the general population.

Children with a significant neonatal history (foetal distress, very low birth weight, very premature infants and exposure to toxins) are at a higher risk of developing mental disorders. Exposure to pre and postpartum complications could increase, in a non-specific way, vulnerability to several types of disorder. The expert group recommends particular attention be paid to children who have been exposed to traumatic events during the ante and post-natal period.

Referral to specialist care

EVALUATION AND FOLLOW-UP IN A SPECIALIST MILIEU OF CHILDREN PRESENTING WARNING SIGNS OF MENTAL DISORDERS OR LEARNING DIFFICULTIES

Children presenting warning signs of autism (developmental delays, language delays, bizarreness, echolalia, and problems with social interaction…) should be referred to diagnosis centres to benefit from assessment. This cognitive assessment of language and communication should include systematic search for neurological factors, caryotyping, metabolic tests, and possibly MRI (nuclear magnetic resonance imaging). The early management of these children constitutes prevention of secondary handicaps. After the pre-school period, a decision must be taken as to whether to refer them for specialist education or not. The expert group recommends developing centres of expertise for the diagnosis of autism and reception centres for the autistic staffed by professionals who have received specific training. There should be a sufficient number of these centres to accommodate children, adolescents and adults.

For children presenting early signs of hyperactivity, there are standardised diagnostic protocols based on research into behavioural profiles. The expert group recommends a systematic evaluation of language and cognitive functions in children presenting signs of hyperactivity as well as systematic research into behavioural disorders, emotional disorders and tics. There are effective treatments, which prevent secondary handicaps.

Children presenting warning signs of obsessive-compulsive disorders (slowness, washing

rituals and fear of contamination, learning difficulties) and/or tics should be followed-up all the more closely if a family history of these same pathologies exists. The expert group recommends performing an assessment in children presenting tics and warning signs of OCD using tools validated for clinical populations in order to establish the diagnosis, along with a systematic search for other disorders, such as depression, which is very frequently associated with OCD.

In adolescents, amenorrhea, weight loss of at least 10 %, sudden changes in weight, excessive preoccupation with body image, food and diet, as well as low self-esteem should be considered as warning signs of anorexic or bulimic behaviour. Other signs such as vomiting, extreme diets or intense physical activity testify to high risk. Monitoring body mass index makes it possible to identify physical risk. The expert group recommends that the medical profession (doctors, paediatricians, gynaecologists, gastro-enterologists…) be made aware of the serious physical and psychological risks inherent in eating disorders, in particular for anorexics who are often referred for treatment very late. The doctor should not hesitate to ask an adolescent girl about her eating habits and think in terms of a rapid referral for psychiatric treatment.

The warning signs of affective disorders (sadness, withdrawal, suicidal notions, a falling off in school results, loss of interest) should be familiar to school nurses and doctors. The expert group recommends that a suicide attempt be systematically considered as a warning sign of an affective disorder. Hospitalisation should provide an opportunity for a visit to a psychiatrist, and also for setting up a follow-up programme by the doctor in charge in association with a psychologist or psychotherapist in order to prevent relapse. Access to medical care for deprived children is insufficient at present. Practitioners are poorly trained in short-term psychotherapy, which can be effective. The number of assessment and treatment centres is too limited.

The warning signs of anxiety disorders (somatic complaints, avoidance, shyness, reserved attitude to adults and other children, sleep disorders, separation anxiety…) are often regarded as trivial and considered transitory by those close to the child. The expert group recommends making access to treatment easier for children presenting the warning signs of anxiety disorders and encouraging the training of those professionals likely to be responsible for the children's care.

The warning signs of schizophrenia (language disorders, psychomotor disorders, affective instability, unexplained angry outbursts, bizarre response to the environment, increased sensitivity in interpersonal relations, difficulties in adjusting to school) are non-specific signs which will expand to include other more specific disorders in adolescence (disorganised thought processes, delirious ideas, hallucinatory phenomena, emotional incongruence...). Schizophrenia in children and adolescents is largely ignored by health care professionals today and little attention is paid to early signs, which leads to late diagnosis. The expert group recommends that particular value be given to training initiatives for medical personnel responsible for the management of patients presenting the warning signs of schizophrenia.

FOLLOW UP WITHIN A SPECIALIST ENVIRONMENT OF CHILDREN PRESENTING MENTAL DISORDERS IN ORDER TO PREVENT THE APPEARANCE OF OTHER DISORDERS

Children presenting certain mental disorders (hyperactivity, OCD, anxiety disorders, learning difficulties…) should be considered as being at risk of developing other mental disorders (affective disorders, anxiety disorders, behavioural disorders) or risk behaviours

(suicide attempts, psychotropic substance abuse…). The period of adolescence and passage to adulthood represent risk periods for the development of an additional pathology for autistic children. Given the significance of comorbidities, the expert group recommends very regular follow-up of children presenting a mental disorder in order to prevent the appearance of another disorder

FOLLOW UP IN THE SPECIALIST MILIEU OF CHILDREN FROM FAMILIES SUFFERING FROM MENTAL DISORDERS

A family history of psychiatric disorders puts an individual at risk of developing the same disorder. Globally, it is possible to distinguish autism, in which genetic determinism is important, (mean heritability of 80 %), then hyperactivity and anorexia nervosa, and finally schizophrenia, affective disorders (especially bipolar disorders for which the significance of family history is at its maximum in the 7-15 year age bracket) and anxiety disorders (mainly OCD and panic disorder) whose heritability is moderate.

Families in which one member is affected by autism, up to 3 generations, should be considered at risk. Each new baby should be followed-up particularly closely in order to be able to benefit from a potential diagnosis and early treatment. Before the age of 2 years, parents play an important role in the identification of disorders and an active part in the interventions organized. The expert group recommends an annual assessment, during the preschool period, of every child coming from a family with a member affected by autism.

A family history of alcoholism, drug abuse or affective disorders should be considered risk factors for the occurrence of mental disorders in the child, disorders which are not necessarily of the same kind. The expert group recommends that health care professionals responsible for adults suffering from a mental disorder pay attention to the psychological development of the children of affected subjects. The expert group also recommends developing preventative activities intended for families, of the same type as those which have already proved effective in the follow-up of children with one parent suffering from a recurrent affective disorder (unipolar or bipolar depression).

Research development

DEVELOPMENT OF TOOLS APPROPRIATE TO THE FRENCH CONTEXT FOR EPIDEMIOLOGICAL STUDIES

Epidemiological studies could benefit from the development of tools for the assessment of mental disorders in children in versions that have been evolved in other countries and validated in France and from training for personnel in the application of these tools. For example, in the case of autism, diagnostic tools exist that can be applied from the first year onwards which should be validated within the French context.

A number of questionnaires for the assessment of mental health in children exist for parents, teacher and young people themselves, as well as numerous scales for the measurement of specific mental disorders. Standardised diagnostic instruments used by trained professionals permit an assessment of mental disorders in a manner compatible with international nosographies. Tools exist as well for measuring risk factors of various kinds (life events, family relationships, and individual characteristics…). The expert group recommends the development of French versions of existing instruments and their standardisation within our

cultural context. Standardisation of these tools, useful for clinical research and epidemiology, necessitates the involvement of professionals for the translation, validation and data collection, as much in outpatient samples as in the general population...). Diffusion of these tools as well as access to training seminars on their application should be made easier for practitioners and researchers in mental health.

DEVELOPMENT OF EPIDEMIOLOGICAL STUDIES ON THE PREVALENCE OF MENTAL DISORDERS IN FRANCE AND THEIR COURSE

An examination of international epidemiological data in psychiatry has for forty years made it possible to detect changes in the incidence of many mental disorders, which could involve various elements (population changes, improved management, modification of nosographic classifications…). The expert group recommends that cross-sectional studies be performed regularly in France across several age brackets of the population to detect secular changes in the incidence of mental disorders.

DEVELOPMENT OF RESEARCH INTO SOCIODEMOGRAPHIC RISK FACTORS FOR MENTAL DISORDERS

Of the sociodemographic determinants, gender and age exert a particular influence on health. Thus, the incidence, expression and even the mechanisms of mental disorders frequently vary according to gender. Boys always seem to be more vulnerable than girls are to developmental disorders. In adolescence, vulnerability in relation to other mental disorders is generally increased in girls. Finally, in adulthood, men more frequently present externalised pathologies, and women internalised pathologies. The expert group recommends the development of studies on gender-specific aetiopathogenic factors (genetic, familial and environmental).

DEVELOPMENT OF COHORTS IN ORDER TO STUDY THE IMPACT OF DIFFERENT EVENTS IN THE COURSE OF THE ANTE AND PERINATAL PERIOD AND CHILDHOOD

The impact of intra-uterine exposure to neurotropic agents (psychoactive substances, synthetic hormones like Distilbene®, environmental toxins) on the child's mental development remains poorly understood. In the same way, the influence and possible mechanisms of action of environmental, social and affective factors during pregnancy have been little studied.

Very low birth weight infants are at high risk of neurodevelopmental disturbances. The expert group recommends that the future mental development of children with very low birth weight be evaluated, including the onset of puberty, by means of cohort studies extending beyond early childhood.

The impact on the child's future of parental mental disorders, both during pregnancy and the first years of life, should be evaluated. For example, the expert group recommends studying the influence on the child's emotional and cognitive development of postpartum depression (defined by DSM-IV criteria) in the mother.

The influence of parent/child interactions (conflicts, educational and emotional inadequacies and inconsistencies) in the occurrence of mental disorders has mainly been the subject of clinical case studies and not of controlled studies. The expert group recommends forming

cohorts in order to evaluate the influence of the quality of exchange between parents and children on the development of mental disorders.

ENCOURAGING STUDIES IN GENETIC PSYCHIATRY TO BE PERFORMED

The weight of genetic factors in mental disorders in children and adolescents, mainly demonstrated in foreign studies, depends in part on the influence of environment (background, study period) on the expression of the genes involved. The expert group recommends the promotion in France of studies of the type involving twins, adoption or follow-up of high-risk children. These studies will allow better definition of the phenotype of the disorders and should be enhanced by other cognitive and psychosocial approaches.

As the various mental disorders are complex and multifactorial, the expert group recommends focussing research in genetic psychiatry on certain homogeneous phenotypical subgroups (for exampleADHD, anorexia nervosa, autism…) whose heritability is over 70 %.

INCLUSION IN THE LONGITUDINAL STUDIES OF NEUROBIOLOGICAL, NEUROCOGNITIVE AND GENETIC RESEARCH MARKERS

Certain disorders in adolescents and young adults are expressed during childhood, but in a way that is almost non-specific or unrecognised. In order to delimit clinical and prodromic syndromes the expert group recommends developing longitudinal studies integrating clinical, psychopathological, neurocognitive measurements and the results of laboratory tests and imaging techniques. The coupling of these endophenotypical studies with those employing genetic markers may also help to delimit syndromes and to identify the components of determinism at its most straightforward. This is a preliminary stage, indispensable to the identification of the aetiological and environmental factors (stress, use of psychoactive substances…) or genetic factors. The course of the deteriorations noted during imaging and their possible modification after intervention could constitute a means of evaluating the methods of management employed (cognitive, pharmacological, learning strategies, stimulations…).

STUDY OF THE GENE-ENVIRONMENT INTERACTIONS IN THE OCCURRENCE OF A MENTAL DISORDER

Exposure to environmental or familial risk factors could promote the expression of a mental disorder in children with a genetic or acquired vulnerability. On the other hand, genetic and environmental protective factors and resilience exist as well.

The expert group recommends incorporating an exploration of genetic vulnerability into the cohort studies, by means of molecular genetic protocols. Straightforward endobuccal sampling has made collecting DNA much simpler, and modern techniques authorise large-scale genetic evaluations.

The expert group also recommends carrying out, within a cohort of children from the general population, followed from birth to the beginning of adulthood, a study of the gene-environment interaction and research into the polymorphisms in some candidate genes in these prospective studies. It recommends an evaluation, for example, of the prospects of using the polymorphism in the gene coding for the dopaminergic receptor D2 *like* (D4) as a diagnostic complement of hyperactivity.

Genetic vulnerability factors are expressed in mental disorders not only in interaction with environmental conditions, but also in all likelihood *via* temperaments that are still poorly understood. The expert group recommends promoting the joint study of several risk factors (temperament, environment, and genetics) and of different markers (neurobiological, neurocognitive and imaging) in order to measure their interactions more effectively.

SETTING UP STUDIES TO DETERMINE THE PREDICTIVE VALUE OF CERTAIN EARLY SIGNS IN THE DEVELOPMENT OF MENTAL DISORDERS

As regards autism, the behaviours observed in the course of the first year of life could provide information on the risk of developing a mental disorder later. The expert group recommends researching behaviours which, during the first months of life, could be the true "precursors" of deteriorated behaviours in the young autistic child.

One of the major difficulties in the early diagnosis of hyperactivity is to distinguish the early manifestations of this pathology from non-pathological psychobehavioural expression connected with development. The expert group recommends the longitudinal study of the development of attention processes and of motor control. The heterogeneous nature of the symptomatic expression and outcome of hyperactivity leads us to promote studies on clinical, cognitive or environmental factors. This research must be part of a multidisciplinary approach combining data from clinical and experimental research.

Children suffering from obsessive-compulsive disorders are difficult to detect before the age of 8-9 years. The child is, in effect, incapable, before this age of describing his pathological thoughts. However, there are non-specific signs such as agitation, withdrawal, aggression and oppositional behaviour, which appear earlier. The expert group recommends studying the predictive value of the non-specific signs observed in children developing obsessive-compulsive disorders.

For eating disorders the period of puberty is a critical phase. The expert group recommends that research be carried out into the risk factors that crystallise at this age (self esteem in connection with body image; perfectionism; addiction, disordered emotional expression) in relation with the occurrence of eating disorders.

As far as schizophrenia is concerned the occurrence of certain disorders in the prepuberty period should alert and make the follow-up and referral of the child possible. The expert group recommends that a study whose aim is to estimate the predictive value of symptoms such as peculiar words or language structure, cognitive disorders, perceptual anomalies and disorders of social adjustment be performed for schizophrenia.

As regards internalised disorders (affective disorders and anxiety disorders) in children and adolescents, their psychosocial effects, their course, at times chronic or recurrent, as well as their significant comorbidity (behavioural disorders, hyperactivity...) command their early recognition and appropriate treatment. Apart from early diagnosis, identification of children and adolescents "at risk" of an affective disorder could be valuable in terms of prevention. The expert group recommends studying, for affective disorders and anxiety disorders, the predictive value of certain early signs sometimes described in the references (inhibited temperament, shyness, excessive emotional reactivity, difficulties with interpersonal relations…) in order to assess the value of systematic detection in the general population and the setting up of preventative activities or early interventions.

The outcome of mental disorders in children or adolescents when they reach adulthood often remains poorly defined. A sufferer may also go from one disorder to another. The timing of the course varies according to the individuals and depends on risk factors and resilience. The

expert group recommends longitudinal follow-up, over the long-term, of children presenting a mental disorder, and that this follow-up takes into account the interventions that have been set up.

EVALUATION OF PREVENTATIVE ACTIVITIES IN GROUPS AT RISK

In children "at risk" of affective or anxiety disorders, preventative actions could be set up, adjusted to existing or recently developed cognitivo-behavioural or systemic programmes. These children "at risk" are those related to subjects already affected, subjects with internalised signs and symptoms, which are still relatively unexpressed, children and adolescents subjected to chronic stress (unfavourable conditions of life, educational failure, conflicts surrounding divorce…). Beyond prevention of disorders of the anxiodepressive spectrum, preventative interventions could also involve more general affective or behavioural dimensions, associated or preceding obvious disorders, such as high-risk behaviours, suicide attempts, relational difficulties or even chronic stress. The expert group recommends an evaluation of preventative programmes of internalised disorders in the populations "at risk" in the French context.

STRUCTURED RESEARCH INTO THE CEREBRAL IMAGING OF MENTAL ILLNESSES

An association of different mental pathologies with developmental anomalies and cerebral maturation seems highly probable, and imaging is one of the best means of bringing it to the fore *in vivo*. However, recruitment of psychiatric patients is generally limited to low numbers and research of this kind often implies the bringing together of standardised information in a longitudinal fashion over time. This could be made easier by centralisation and the creation of regional banks of imaging data, in, or close to, centres that bring together those competent to analyse them. The expert group recommends, prior to the evaluation of imaging in the area of early diagnosis of targeted pathologies, the setting up of image databanks. In the case of certain disorders without associated neurological signs (dyslexia, autism, anorexia with a certain severe undernourishment) the expert group recommends studying the contribution that anatomical and functional imaging has made to diagnosis.

RESEARCH INTO THE MECHANISMS UNDERLYING MENTAL DISORDERS

Anatomical, functional and metabolic imaging and the study of neurotransmitters and functional cognitive anatomy may help to understand the aetiopathogenic mechanisms underlying mental disorders. In the course of precise mental tasks, different cerebral imaging techniques permit detection of the existence of anomalies in the functioning of the neuron networks implicated in the mental activities examined.

Modifications in cerebral functioning associated with deteriorations in cognitive function were brought to the fore in autism, certain anxiety disorders such as obsessive-compulsive disorder, or in attention disorders such as hyperactivity in children. Psychotic or depressive disorders (schizophrenias) or those of cerebral function, currently being explored by anatomo-functional imaging in adults, are little studied at the time of their inception in young people. A study of these negative changes or deviations in blood flow, regional metabolic activity, electrophysiological activity collected by evoked potentials, during cerebral development and in the course of these disorders, is an indispensable step in understanding their physiopathology.

The expert group recommends increasing our knowledge about the putting into place and physiological maturation of neurocognitive systems, in order to research the mechanisms underlying their dysfunction. In the same way, it recommends defining and locating the effects of medicines according to the clinical behavioural modifications observed.

DEVELOPMENT OF ANIMAL MODELS OF DEVELOPMENTAL ANOMALIES

The physiopathological cerebral mechanisms implicated in the connection between early neurodevelopmental disturbances and an increased vulnerability in relation to psychiatric disorders remain poorly understood. It involves the impact of the processes of cerebral maturation, in particular in the course of adolescence, on these early neurodevelopmental disturbances. Studies often omit the changing dimension of mental disorders in children, in relation to the idea of neuronal plasticity. Certain experimental modules, animal and cellular, have been developed in order to understand the physiopathological mechanisms at the molecular or cellular level. Recent animal research has thus permitted modifications, notably of our theoretical concepts and knowledge of the mechanisms of neuronal reorganization in the course of development as in the course of postnatal life. In addition animal models allow us to apply the knowledge acquired on the genetic and molecular levels, and to test certain therapeutics, in particular those acting on the development and perpetuation of disorders. Moreover, research into new markers of the different psychopathologies in children makes it possible to propose new aetiopathological hypotheses, which can be tested in animals.

The expert group recommends the development of animal models of developmental anomalies and their exploration by neurobiological and behavioural methods as well as by cerebral imaging. This research would benefit from a coming together of developmental and behavioural neurobiologists, and in general from collaboration between clinical and fundamental research.